SURGICAL BACTERIOLOGY.

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EXCERPTED FROM

A SYSTEM OF SURGERY.

BY AMERICAN AUTHORS.

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GENERAL BACTERIOLOGY OF SURGICAL INFECTIONS.

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Members of each of the three groups of pathogenic micro-organisms —bacteria, fungi, and protozoa—may cause surgical infections. Fungi and protozoa, however, are far less commonly concerned in these infections than are bacteria. In a general consideration of the conditions of surgical infection bacteria are the organisms which require chief attention, so that the subjects to be considered in this article can be appropriately included under the designation "General Bacteriology of Surgical Infections."

The term "general bacteriology" is here used in distinction from "special bacteriology" to designate the general relations of bacteria to surgical infections. It is not deemed necessary in this article to enter into a detailed consideration of the morphological and cultural characters of bacteria. This subject is fully treated in works especially devoted to bacteriology.

Infectious diseases which require especial consideration by the surgeon include, on the one hand, many specific infections, such as tuberculosis, tetanus, glanders, anthrax, and actinomycosis, and, on the other hand, traumatic and other inflammatory and septic infections caused by various widely-distributed bacterial species.

The specific infectious diseases, such as tuberculosis, tetanus, etc., are for the most part sharply differentiated by their anatomical and clinical characters, and are caused by micro-organisms which are constantly and exclusively associated with their respective diseases.

On the other hand, the common traumatic infections and other surgical inflammations and septic processes do not present equally sharp and definite differential characters, and apparently identical or similar pathological processes belonging to this group of affections may be caused by various micro-organisms. Thus we do not find in such diseases as septicæmia, pyæmia, abscesses, osteomyelitis, puerperal fever, or other septic and localized inflammations, or, in general, in the infections of wounds, any single bacterial species constantly and exclusively associated with each of these affections, but each disease of this group may be caused by more than one species of micro-organism.

The etiology of these common septic and inflammatory affections presents for our consideration many problems quite distinct from those pertaining to the causation of the specific infections. The views now held as regards sources of infection, operative procedures, and the management of wounds have been developed largely as the result of investigations concerning the relation of bacteria to traumatic infections.

It is important that the surgeon should become familiar with the various kinds of bacteria concerned in surgical infections, with their distribution on exposed surfaces of the body and in the outer world, with the ways by which they may enter and be discharged from the body, with the various conditions which favor their invasion and multiplication in the body, with their pathogenic manifestations, and with the means of combating them. It is proposed in this article to present the more important considerations pertaining to these subjects so far as they do not fall more appropriately for their treatment to other sections of this work.

We shall consider first the distribution of bacteria on exposed surfaces of the body, having especially in view its surgical bearings. Knowledge of the distribution of pathogenic bacteria is of importance in the study of the causation of surgical infections, as indeed of all infectious diseases.

Bacteria of the Skin.

There are various questions of surgical interest relating to the bacteria of the skin. The destruction of the surface bacteria both on the hands of the operator and his assistants and over the field of operation in the patient is of fundamental importance in surgical technique. It is important to determine the possibilities of danger from infection by bacteria commonly or occasionally found in or on the skin. Ignorance of the bacterial flora of the normal skin has led some investigators to erroneous interpretations of their observations as to the source of bacteria found in wounds treated aseptically or antiseptically, and as to the presence of supposed specific pathogenic bacteria in certain cutaneous diseases.

The micro-organisms of the human skin have been studied by several investigators, of whom may be mentioned Bizzozero, Bordoni-Uffreduzzi, Unna, Maggiora, Mittmann, Fürbringer, Preindlsberger, Robb and Ghriskey, and Welch.[1]

As the skin is exposed to contamination from the air and all sorts of sources, it is evident that there is scarcely any limit to the number of species of bacteria which may possibly be found on the skin. Most investigators of this subject have not had the patience or have not thought it worth while to attempt to identify or to describe all of the various kinds of bacteria developing in cultures from the surface of the skin. Mittmann mentions seventy-eight different species of cutaneous bacteria, of which fifty-six were cocci. His descriptions, however, are so imperfect as scarcely to serve for the identification of the species. Preindlsberger describes thirty-two species, of which twenty-eight were cocci. Maggiora isolated twenty-nine micro-organisms, of which twenty-two were bacteria, three budding fungi, and four moulds. Most of these bacteria are such

[1] Bizzozero, *Virchow's Archiv*, Bd. 98; Bordoni-Uffreduzzi, *Fortschritte der Medicin*, 1886, p. 151; Unna, *Monatshefte für praktische Dermatologie*, 1889, 1890, 1891; Maggiora, *Giornale della R. Società d'Igiene*, 1889; Mittmann, *Virchow's Archiv*, Bd. 113; Fürbringer, *Desinfektion d. Hände d. Arztes*, Wiesbaden, 1888; Preindlsberger, *Zur Kenntniss der Bacterien des Unternagelraumes u. s. w.*, Wien, 1891; Robb and Ghriskey, *Johns Hopkins Hospital Bulletin*, April, 1892; Welch, *Trans. of the Congr. of American Physicians and Surgeons*, vol. ii., and *Maryland Medical Journal*, Nov. 14, 1891.

as are often found in the air or on external objects. Cocci are usually found much more abundantly than bacilli in cultures from the skin.

Great variations exist in different cases as to the kinds and the number of bacteria found on the skin. Sometimes one species predominates over the rest, indicating that it has multiplied and overgrown other bacteria. The conditions in general are not favorable for the growth of bacteria on the surface of the skin, but under the nails and in situations where moisture collects, as in the axillæ, the groins, and between the toes, there may be abundant multiplication of certain species of micro-organisms. Although bacteria predominate, budding and mould fungi are often present. The large number of micro-organisms which accumulate beneath the nails is a matter of surgical importance. From a minute particle of material from this situation sometimes as many as two thousand to five thousand colonies develop in culture media, although usually the number is much less, and may be very small indeed, perhaps not more than three or four colonies.

The writer in 1891 was the first to call attention to the fact that, although in general the bacterial flora of the skin is inconstant and indefinite in its special characters, there is one bacterial species, to which he gave the name of *staphylococcus epidermidis albus*, which is found with such regularity in cultures from the skin that it may properly be regarded as a regular inhabitant of the normal skin, just as the bacillus coli communis is a regular inhabitant of the intestinal canal. The principal data relating to this staphylococcus were established by the researches of Robb and Ghriskey. We consider this coccus to be a variety of the staphylococcus pyogenes albus. It is possessed of feeble pyogenic power, and usually liquefies gelatin and coagulates milk more slowly than the ordinary white pyogenic staphylococcus. For these reasons, but especially to emphasize the epidermis as a normal habitat for this organism, we applied the designation mentioned.

One of the chief points of interest relating to this coccus is that it is very often, probably regularly, present in layers of epidermis along the hair-shafts, deeper than can be reached by any known means of cutaneous disinfection save the application of heat. After complete sterilization of the surface of the skin, so that scrapings are sterile when inoculated into culture media, the presence of this white coccus can still be demonstrated by making cultures from sutures passed through the skin or from excised pieces of skin.

The staphylococcus epidermidis albus is usually innocuous. It is found frequently in aseptic wounds of the skin without causing suppuration or any trouble. The source of this coccus in aseptic wounds does not seem to be known to many who have made bacteriological examinations of such wounds; thus Büdinger,[1] who examined in 1892 twenty operative wounds which healed by first intention in Billroth's clinic, could not suggest any other origin for its presence than the air, and C. Fraenkel[2] suggests that it is brought to the wound by the blood-current—suggestions which were rendered quite unnecessary by our previous researches.

Although this white epidermal staphylococcus is often found in wounds without any disturbance in the process of healing, it may be

[1] Büdinger, *Wiener klin. Wochenschr.*, 1892, Nos. 22, 24, 25.
[2] C. Fraenkel, *Baumgarten's Jahresbericht*, 1892, p. 28.

the cause of some disturbance, characterized especially by elevation of temperature and moderate suppuration. This is particularly likely to be the case when there is necrotic or strangulated tissue in the wound or when foreign bodies have been introduced into the wound. It is a common, although not the sole, cause of stitch-abscesses, and it is prone to travel down along the sides of a drainage-tube, and under these circumstances may cause the wound to suppurate. It is often associated with other pyogenic cocci in cutaneous inflammations. We can now understand how, without any flaw in the antiseptic technique of the surgeon, this micro-organism may be present in wounds, and we have a satisfactory explanation of the frequent occurrence of stitch-abscesses.

This white skin-coccus is often present in cultures from blood obtained by puncture of the human skin and in cultures from the sweat after complete disinfection of the surface of the skin. Some observers seem to have supposed that when the staphylococcus albus is demonstrated under these conditions its presence in the circulating blood or its excretion by the sweat-glands can be inferred. But it is evident that such an inference is unwarranted without additional proof.

There are various other white cocci, and also several species of yellow cocci, both liquefying and non-liquefying, which are frequently found in cultures from the skin. Some of the yellow cocci can readily be mistaken for the staphylococcus pyogenes aureus, unless they are carefully studied in culture media. The staphylococcus pyogenes aureus may be found on the skin, as will be mentioned presently.

The kinds and the number of bacteria found upon exposed parts of the skin vary considerably according to the habits and the occupation of the individual. Of especial interest in this connection are the results of the examination of the skin of surgeons and others who come into contact with infected persons either during life or at the autopsy-table. We have found only exceptionally the *staphylococcus pyogenes aureus* upon the hands of those who do not come into proximity to surgical or infected cases, whereas we have many times found this micro-organism upon the hands of surgeons, their assistants, and surgical nurses. In examining the hands of those who use corrosive sublimate as a disinfectant it is necessary first to neutralize the sublimate with ammonium sulphide, as we have found that the sublimate may prevent the development of cutaneous micro-organisms with which it has come into contact, although it has not killed them ; and this restraining influence may be manifest days, and even weeks, after the application of the sublimate.

The length of time that the yellow pyogenic staphylococcus may persist upon the hands varies, and doubtless largely, according to the methods and extent of cleansing the skin. It certainly may persist for several days, although it may disappear in a few hours. It does not seem usually to grow down, as does the white epidermal coccus, into the deeper layers of the skin, so that ordinary methods of disinfection of the skin are likely to remove or destroy this organism. By rubbing or by the application of pressure the staphylococcus aureus may, however, be pressed into the deeper layers, particularly into the hair-follicles, and there cause furuncles, as has been shown by the experiments of Garré, Schimmelbusch, Wasmuth, and others. The view which has been advocated by some writers that it requires more thorough disinfection to

remove or destroy pathogenic bacteria accidentally or intentionally applied to the skin than to kill the ordinary bacteria of the skin is not supported by experiments. The healthy skin in general is not a favorable resting- or breeding-place to secure the long persistence of pathogenic bacteria, with the exception of the white epidermal coccus, which possesses relatively little pathogenic power under ordinary circumstances.

The *streptococcus pyogenes* has been found less frequently than the staphylococcus aureus in cultures from the skin, and here too chiefly in cultures from the skin of infected patients or of those who have been in proximity to them. It is well to bear in mind that these pyogenic cocci are not necessarily limited to the immediate neighborhood of an infected wound or focus, but may occur on other parts of the body, as well as in the air or on objects which have been near the patient. Thus Preindlsberger found the aureus in the dirt beneath the finger-nails of a patient with fracture of the femur, and the streptococcus pyogenes in the same situation in a patient with osteomyelitis femoris for which necrotomy had been performed. The complete disinfection of an infected wound, even if that were possible, would not therefore furnish a guarantee that pyogenic cocci were not present upon the surface of the patient's body in other situations.

The *bacillus pyocyaneus* is a common parasite upon the human skin. Mühsam[1] found it in the axilla and in the anal and inguinal folds of healthy persons in 50 per cent. of the cases examined. Probably local conditions were concerned in these observations, as others have not found this organism upon the healthy skin with such frequency. Although this organism may manifest important pathogenic activities, its presence in wounds is usually made evident chiefly by the green or blue discoloration of the dressings. It was formerly supposed to enter the wound from the air, but it doubtless is often derived also from the skin of the patient.

The common intestinal bacterium, the *bacillus coli communis*, is of course often present on the skin about the anus. In abscesses in this situation it is often found either alone or associated with other bacteria. The colon bacillus may also be found upon the skin in other parts of the body. It is a widely-distributed bacterium outside of the animal body. It has repeatedly been found in wounds in different parts of the body.

Skin contaminated with the soil, which, as is well known, contains in many situations abundant bacilli of tetanus and of malignant œdema, is likely to present these micro-organisms. This contamination relates, of course, especially to the hands, and in the case of those who go barefoot or have holes in their shoes also to the feet. Maggiora was able to demonstrate the bacillus of malignant œdema in scrapings from between the toes of a person who had walked for half an hour in a garden with a torn shoe. It is not therefore in all cases necessary to suppose that the tetanus bacillus enters a wound from the object which causes the wound, for this bacillus may previously have been attached to the skin. It may in this connection be mentioned that the fæces of herbivorous animals often contain the tetanus bacillus, and in a condition more

[1] Mühsam, cited by Schimmelbusch, *Samml. klinischer Vorträge von Volkmann*, Serie 3, Heft. ii. No. 62.

likely to produce tetanus than when the bacillus is obtained from the soil. Buday[1] has reported a case of tetanus fatal in twenty-four hours which followed the smearing of a wound with fæces.

The *smegma bacillus* may be considered in connection with the cutaneous bacteria. This bacterium is usually present in the smegma, and may be found about the penis, scrotum, vulva, and anus. Attention was first called to this bacillus by Alvarez and Tavel and by Matterstock in 1885, on account of its resemblance in morphology and staining reactions to Lustgarten's bacillus, which at that time was thought by its discoverer to be the specific cause of syphilis. Greater practical importance, however, belongs to the smegma bacillus at present on account of the possibility of mistaking it from its staining properties for the tubercle bacillus, and there is reason to believe that such mistakes have been made in examinations of the urine and of secretions or exudates about the external genitals and the anus. The smegma bacillus resembles the tubercle bacillus in the property of retaining the staining dye after such application of acids and alcohol that all known bacteria except the tubercle bacillus, the smegma bacillus, and the leprosy bacillus are decolorized. This property probably does not inhere in the smegma bacilli as such, but is due to the presence of chemical constituents of the smegma, although this point is not positively settled. In the opinion of the writer this peculiar staining reaction does not belong to only a single species of bacillus in the smegma, but to several, so that it is more proper to speak of smegma bacilli with this reaction. Mistakes are particularly likely to occur when the handy and popular Gabbet's stain for the tubercle bacillus is employed. The usual statement is that the smegma bacilli can be distinguished from the tubercle bacillus by less resistance to decolorizing agents, particularly to nitric acid, hydrochloric acid, and alcohol, also to counter-stains; and this often holds true. Nevertheless, smegma bacilli are sometimes encountered which are as resistant to these decolorizers as are tubercle bacilli. Especial attention should be given to the morphological appearances, as the size and shape of the bacilli often suffice for the distinction, although there is considerable diversity as regards this feature between the different smegma bacilli which resist decolorization. Although smegma bacilli may be present with pathogenic bacteria in lesions around the genitals and anus, they are not known to possess pathogenic capacity.

Many bacteria are attached to the hairs of the body, and particles containing bacteria may readily be detached from the hair. Robb has studied the bacteria which fall off from the hair of the head by movement or by combing the hair. They are identical with those found on the skin, as might be expected. Haegler has cultivated pyogenic staphylococci from the hair of surgeons, and calls attention to the possibility of such cocci falling from the hair into a wound or upon objects coming into contact with the wound during an operation. Wright has found the diphtheria bacillus on the hair of nurses in attendance on cases of diphtheria.

The cerumen is rich in bacteria. Rohrer[2] isolated sixteen species of micro-organisms from the cerumen of fifty cases, but he has not attempted

[1] Buday, *Pester Med.-chir. Presse*, 1894, No. 19.
[2] Rohrer, *Archiv f. Ohrenheilk.*, Bd. xxix.

to identify any of these with previously-known bacteria, and his statements as to the existence of pathogenic bacteria in the cerumen are not based upon conclusive observations.

Bacteria of Exposed Mucous Surfaces.

The way is open for the access of micro-organisms to mucous membranes which cover parts which communicate with the outer world through the external orifices of the body. So far as temperature, moisture, and the presence of nutritive pabulum are concerned, the conditions are manifestly more favorable for the growth of bacteria upon mucous surfaces than upon the dry skin. These relatively favorable conditions for the development of micro-organisms upon mucous membranes are, however, counteracted in large measure by various mechanical and chemical influences which prevent the prolonged survival of most of the bacteria which may enter through the external orifices of the body. There are, however, many bacteria which may multiply, or persist for a long time or indefinitely, upon certain mucous membranes in health, particularly those of the alimentary canal and of the upper respiratory tract, and there are some bacterial species which find their natural home here. Some pathogenic bacteria may live upon certain mucous membranes without doing harm.

The study of the bacterial flora of exposed mucous membranes in health and in disease has brought to light many points of surgical interest.

Conjunctiva.—The bacteriology of the conjunctiva has been investigated by many ophthalmologists, of whom may be especially mentioned Fick, Weeks, Leber, Felser, van Genderen Stort, Gombert, Bernheim, Hildebrandt, Franke, Marthen, and Bach.[1]

When one considers the exposed situation of the conjunctiva, it is surprising to find how small is the number of bacteria usually present in the conjunctival sac. Fick found, by microscopical examination of fifty healthy conjunctivæ, bacteria in only eighteen, although in another series in which forty-nine healthy eyes of paupers were examined bacteria were missed in only six. A negative microscopical examination, however, indicates only that the number of bacteria is small, as then their presence may readily be overlooked without the aid of cultures. As a matter of fact, cultures from the healthy conjunctival sac usually furnish colonies of bacteria. Their number may be considerable, but it often happens that not more than three or four colonies develop from a loopful of fluid from the conjunctiva, and it is not very uncommon for culture media inoculated in this way to remain sterile. It is to be assumed that the conjunctival sac ordinarily contains bacteria. The secretion within the lachrymal glands is sterile.

Bach describes twenty-six species of bacteria isolated in pure culture from the healthy or diseased conjunctiva. Of these, ten are liquefying cocci, nine non-liquefying cocci, five liquefying bacilli, one non-liquefying bacillus, and one cladothrix. Ten of the twenty-six bacteria were found to be more or less pathogenic when inoculated into the rabbit's cornea.

[1] L. Bach, "Ueb. d. Keimgehalt des Bindehautsackes," *Archiv f. Ophthalmologie*, Bd. xl. p. 130. This article contains the references to the other articles cited in the text.

Pink yeast and mould fungi have also been cultivated from the conjunctiva.

Bach considers that of these various bacteria only the staphylococcus pyogenes aureus and albus and the streptococcus pyogenes are demonstrated to be pathogenic for man, although the possibility that others in the list may be pathogenic for man must be admitted. In a few instances the staphylococcus pyogenes aureus, and in more the albus, have been cultivated from the healthy conjunctiva. Cultures of the staphylococcus pyogenes aureus have been introduced into the healthy conjunctival sac of man and animals without causing inflammation.

Inasmuch as many micro-organisms must enter the conjunctival sac from the air, the edges of the eyelids, and from contact with the fingers and other objects, and as relatively few bacteria are found ordinarily in cultures from this part, it is evident that there must be some very efficient mechanism which rids the conjunctiva of most of the bacteria which enter. There are two principal agencies by which this may be accomplished—namely, mechanical removal through the naso-lachrymal duct, and the germicidal action of the lachrymal and conjunctival secretions. Some investigators have attached the greater importance to the former, others to the latter, of these agencies. Experiments have shown that each may be operative, but the mechanical removal has been shown to be especially efficient and prompt in its action.

Van Genderen Stort has made experiments upon rabbits, and Bach upon man, by dropping pure liquid cultures of easily-identified bacteria, such as the Kielwater bacillus, the bacillus coli communis, the staphylococcus aureus, into the conjunctival sac, and then determining by cultures the length of time during which they can be demonstrated. Van Genderen Stort found after fifteen minutes the inoculated bacteria reduced to a small number, and at the end of an hour they had nearly or entirely disappeared from the conjunctival sac. Cultures from the nose showed that they had been carried down the naso-lachrymal duct, and that after five minutes they were abundant in the cultures from the nasal cavity. Identical results were obtained by Bach in his experiments on human beings. In the experiment of Bach with the staphylococcus aureus, however, which was introduced in such number that the immediate plates from the conjunctiva contained countless colonies, there were still seventy-four colonies in the plates made after twenty-four hours.

The same experiments were made after ligation of the naso-lachrymal duct. Under these circumstances the inoculated bacteria also disappeared from the conjunctival sac, but more slowly than when the duct was open. Still, after an hour most of the bacteria had been removed. It was found that they had been carried away by the lachrymal secretion which flowed over the eyelids. If the eyelids were closed by a bandage, the bacteria, with open nasal duct, rapidly passed down into the nose, and they did not appear to pass out between the closed eyelids. When, however, the duct was closed, they appeared abundantly in the bandage.

Bernheim has demonstrated that the tears possess considerable bactericidal power over certain species of bacteria, and his results have been in part confirmed by the experiments of Marthen, Bach, and others. The staphylococcus pyogenes aureus is killed in moderate number, and the typhoid bacillus in larger number, by the lachrymal secretion. We

must therefore assign importance to this chemical action, as well as to the mechanical removal, in ridding the conjunctiva of invading bacteria. Neither of these agencies suffices to remove all of the bacteria. Some bacteria grow readily in the fluid of the conjunctiva. As has already been mentioned, the conjuctiva nearly always contains some bacteria. The orifices of the Meibomian glands, the cilia, and the edges of the eyelids usually contain many bacteria, and these of course may readily enter the conjunctival sac.

Bach was unable to demonstrate that bacteria introduced into the nasal cavity ever make their way up the nasal duct to the eye.

It is difficult to obtain complete disinfection of the conjunctival sac. The number of bacteria may be greatly reduced, either by the application of antiseptics or by simple mechanical cleansing, combined with irrigation by an indifferent fluid, such as sterilized salt-solution. Bach obtained the best results by the latter procedure, by which in sixteen out of forty-two cases he rendered the conjunctiva sterile.

The importance of familiarity with the saprophytes to be found on exposed mucous membranes is illustrated by the history of the so-called xerosis bacillus. This bacillus was discovered by Neisser in 1882 in xerosis of the conjunctiva, and was regarded by him as the cause of this disease. This conclusion was adopted by several subsequent investigators, who found this bacillus constantly present in xerophthalmia. This same bacillus has, however, been demonstrated by Schreiber, working under Neisser's direction, in various other affections of the eye, and also, although in small number, in the normal conjunctival sac. Neisser has therefore given his assent to the conclusion expressed by Schreiber:[1] "The so-called xerosis bacilli are to be regarded as saprophytes which are often present in the conjunctiva and its secretion, both in diseased and healthy eyes, and they play no special rôle either in xerosis or in other diseases of the eye."

The xerosis bacillus belongs to an interesting group of bacteria which are characterized by remarkable irregularities in size and shape—so-called involution forms—and by irregularities in staining, especially by the presence of deeply-staining isolated granules. It is not positively proven to form spores, although some of the isolated granules are interpreted as such by Ernst and by Neisser. To this same group belong the diphtheria bacillus of Löffler and the so-called pseudo-diphtheria bacilli.

Mouth and Pharynx.[2]—All of the micro-organisms which may be present in the air, food, and ingested fluids may appear temporarily in the mouth. The number of bacteria which have been cultivated from the human mouth is very large. Miller has isolated over one hundred species. Freund has cultivated eighteen different chromogenic micro-organisms from the mouth.

It is important to distinguish between the countless bacteria which may appear as transient visitors in the mouth and those which find their permanent home there. A remarkable peculiarity of the constant inhabit-

[1] Schreiber, *Fortschritte der Medicin*, 1888, p. 656.

[2] Miller, *Die Mikro-organismen der Mundhöhle*, Leipzig, 1889; David, *Les Microbes de la Bouche*, Paris, 1890. These valuable works present the most important results hitherto obtained by the investigators of the micro-organisms of the mouth.

ants of the saliva is that most of them will not grow in our artificial culture media. This produces often a striking discrepancy between the results of microscopical examination of the buccal secretions and those obtained by cultures. Cover-slip specimens may show an enormous number of bacteria, when cultures made from the same material may show very few or even no colonies.

Miller enumerates the following as the constant buccal bacteria: *leptothrix buccalis innominata, bacillus buccalis maximus, leptothrix buccalis maxima, iodococcus vaginatus, spirillum sputigenum, spirochæte dentium*. None of these have been artificially cultivated. Bacillus buccalis maximus and iodococcus vaginatus are stained violet by iodine solution. These bacteria are often present, with others, in carious teeth, in abscesses communicating with the mouth and pharynx, and in exudates on the mucous membranes of these parts, but they have not been proven to be pathogenic.

The frequent presence of pathogenic bacteria in the healthy mouth is of great practical importance. The following pathogenic bacteria have been found repeatedly in this situation: *micrococcus lanceolatus, streptococcus pyogenes, staphylococcus pyogenes aureus* and *albus, micrococcus tetragenus, bacillus pneumoniæ* of Friedländer, *bacillus crassus sputigenus* of Kreibohm, *bacillus coli communis*. Biondi, Miller, Kreibohm, Galippe, and others have found in the mouth additional pathogenic bacteria in isolated cases, mostly, however, with some morbid condition.

The micrococcus lanceolatus was discovered by Sternberg in his saliva in 1880. Many names have been given to this bacterium, the more common synonyms being diplococcus pneumoniæ, pneumococcus of Fraenkel and Weichselbaum, diplococcus lanceolatus, micrococcus of sputum septicæmia, and micrococcus pneumoniæ cruposæ (Sternberg). This micro-organism was found by Netter in a virulent condition in 15 to 20 per cent., of the healthy persons whom he examined. It varies markedly in virulence, and it is probably present in a non-virulent condition in many cases. Indeed, Kruse and Pansini believe that the micrococcus lanceolatus is a regular inhabitant of the human mouth, although it is present in a virulent state in only about one out of five or six persons. As the lanceolate coccus, especially when its virulence is weak or absent, may grow in chains and present cultural characters of the streptococcus pyogenes, it is often difficult, if not impossible, to distinguish between these bacteria.

The chief interest attaching to the frequent presence of the micrococcus lanceolatus in the healthy mouth is that this bacterium is the cause of lobar pneumonia and of many cases of broncho-pneumonia. It may also be concerned in local inflammations of the throat, and as a primary or secondary invader may cause serositis and localized inflammations in various parts of the body; but the streptococcus pyogenes is a more common cause of these lesions.

Various virulent and non-virulent streptococci have been found in the mouth, both short-chained streptococci and long-chained forms, corresponding to the two varieties, streptococcus brevis and streptococcus longus. The distinctions upon which these varieties were established by Von Lingelsheim are often inconstant, and do not serve for a sharp differentiation. The chief interest belongs to the presence in the mouth

and pharynx of the streptococcus pyogenes. Netter found the streptococcus pyogenes in seven out of one hundred and twenty-seven healthy mouths examined; that is, in 5.5 per cent. of the cases. Dörnberger found streptococci in the mouths of healthy children in 45 per cent. of the ninety-four cases examined. Widal and Besançon found streptococci constantly and in large number in the mouths of twenty healthy persons, and still more abundantly in the mouth and pharynx of forty-nine persons affected with various diseases.

It often requires a painstaking examination to detect this streptococcus. The colonies are minute and pale gray, and in a plate crowded with other more striking colonies the former may escape recognition unless especial attention is given to them. If the secretions of the healthy mouth and throat be carefully examined both by cover-slip preparations and by agar plate-cultures, streptococci will be found with great frequency, if not regularly, although, as already mentioned, it is by no means easy to distinguish some of the streptococci from chain forms of the micrococcus lanceolatus.

The number of streptococci is increased and their detection is much easier in most inflammatory conditions of the tonsils and pharynx. They are commonly associated with the diphtheria bacillus in diphtheria, and they are capable of causing all grades of tonsillitis and pharyngitis, from slight erythematous forms to pseudo-membranous and necrotic inflammations.

Streptococci cultivated from the healthy mouth usually have little or no virulence as tested upon animals, and the same is often true of streptococci cultivated from the throat in various infections, local and general, although in these cases they are more likely to be pathogenic for animals.

The streptococcus pyogenes is a common and dangerous invader of the deeper air-passages and lungs and of the internal parts of the body. The portal of entry is often the tonsils and throat, and predisposing causes are inflammations and other lesions of these parts, particularly when combined with other infectious diseases and constitutional disturbances. Under conditions little understood the mouth-streptococci may acquire enhanced virulence.

The influence of predisposing causes as a factor in the etiology of infections is well exemplified by the fact that healthy mucous membranes harbor very frequently such pathogenic germs as the micrococcus lanceolatus and the streptococcus pyogenes. These bacteria often, moreover, cause no serious disturbance in the repair of wounds and injuries involving the mouth and naso-pharynx, although they must gain access to such wounds. They are, however, a standing menace in surgical operations involving these parts, and they may seriously interfere with the healing of such wounds, or may under these circumstances set up pneumonia and general infection.

Staphylococci are found often in the healthy mouth and the throat, but the genuine pyogenic staphylococci do not appear to be present with great frequency. Vignal, Netter, and Miller met the staphylococcus pyogenes aureus only in a comparatively small number of cases in their bacteriological examinations of the healthy mouth. It is found more frequently in various inflammations of the mucous membranes of this

region, but it plays no such important rôle in these as does the streptococcus pyogenes.

White liquefying cocci, often described as the staphylococcus pyogenes albus, are found oftener than the staphylococcus aureus in the mouth and throat. Some of these have been shown to possess pyogenic power, and may be accepted as the staphylococcus pyogenes albus, but others are devoid of such power.

According to the statements of Biondi, Miller, and others, the micrococcus tetragenus, which was discovered by Koch and Gaffky in a phthisical cavity, is often present in the mouth. In a considerable number of cases examined by the writer it was absent. The frequency with which certain bacteria are present in the mouth probably varies considerably in different regions and according to the class of cases selected for examination. There are various species of tetragenous cocci. The pathogenic form of Koch and Gaffky is designated by Boutron as micrococcus tetragenus septicus. This organism is present more frequently in abscesses in the neighborhood of the mouth and throat, particularly those connected with carious teeth, than in abscesses in other parts of the body, although even in the former it is rarely present.

The virulent diphtheria bacillus was found by Park and Beebe[1] in the healthy throats of eight out of three hundred and thirty persons in New York who gave no history of direct contact with cases of diphtheria. Only two of these eight persons afterward developed diphtheria. They found non-virulent, but otherwise characteristic, diphtheria bacilli in twenty-four throats of the same group of persons, and pseudo-diphtheria bacilli in twenty-seven.

The pseudo-diphtheria bacillus which is occasionally found in the throat is devoid of virulence, and presents certain cultural peculiarities distinguishing it from the genuine diphtheria bacillus. It is not known to be pathogenic. There is much confusion in the use of the term "pseudo-diphtheria bacillus," and some writers have described under this name the genuine diphtheria bacillus devoid of virulence. There is probably more than one bacterial species which may be called pseudo-diphtherial bacillus.

The mouth and adjacent parts are the most frequent portals of entry of the bacterium of actinomycosis. This organism is likely to lodge near carious teeth.

Although the mouth and throat offer more favorable conditions for the prolonged existence of many micro-organisms than do other exposed mucous membrane, nevertheless of the vast hordes of micro-organisms which must gain access to the mouth only a small number actually persist there. The conditions are evidently unfavorable for the survival of the majority of bacterial species in this situation. Those which are unable to gain a foothold must sooner or later pass down into the stomach or intestine or out through the mouth and nose or perish within the body.

The secretions in the mouth and throat, like most of the fluids of the body, possess some degree of germicidal power. Sanarelli[2] found that the saliva is capable of killing in a short time a moderate number of

[1] Welch, "Bacteriological Investigations of Diphtheria in the United States," *Am. Journ. of the Med. Sciences*, Oct., 1894.

[2] Sanarelli, *Centralbl. f. Bakter.*, 1891, Bd. x.

several pathogenic bacterial species. This was found to be the case with the staphylococcus aureus, the streptococcus pyogenes, the micrococcus tetragenus, the typhoid bacillus, and the cholera spirillum. The diphtheria bacillus, however, survived for twenty-eight to forty days, and the micrococcus lanceolatus grew well in saliva, although with rapid loss of virulence.

E. Grawitz and Steffen[1] have confirmed this observation of Sanarelli as regards the pneumococcus, and have found that the virulence of this organism may be restored by cultivating it upon pneumonic sputum prepared as an artificial culture medium. They interpret this as indicating that the virulence of the pneumococcus may be enhanced by certain chemical changes in the composition of the sputum.

There is reason to believe that the virulence of pathogenic bacteria in the mouth, notably of the micrococcus lanceolatus and the streptococcus pyogenes, may fluctuate, both in the direction of attenuation and of exaltation, but we are not acquainted with the conditions which control these changes.

The salivary glands and ducts are free from bacteria, except near the orifice of the ducts.

Respiratory Passages and Middle Ear.—In normal respiration the bacteria contained in the inspired air must enter the nasal cavities. The anatomical arrangement of the nasal passages renders these an important filtering apparatus for the protection of the deeper air-passages. It has been shown by experiments of Wright that with a respiration of one litre of air per minute from three-fourths to four-fifths of the bacteria of the inspired air are retained in the nasal cavities and their adnexa.

It has already been mentioned that most of the bacteria which enter the conjunctival sac are carried into the nose through the nasal duct. We should therefore expect that the nasal cavities would contain abundant micro-organisms.

The bacteria of the healthy nose have been studied by E. Fraenkel, Loewenberg, Hajek, von Besser, Wright, Paulsen, Weibel, Deletti, and others, with much divergence in their results. Some have found few, others many, bacteria in the nose; some have met frequently pathogenic bacteria, others rarely or not at all.

Von Besser[2] describes twelve non-pathogenic species isolated from the noses of thirty persons at work in the laboratory. In the same group of cases he found in the nose the micrococcus lanceolatus six times, the streptococcus pyogenes five times, the staphylococcus pyogenes aureus seven times. In the nasal cavities of twenty-eight convalescent hospital patients he found the micrococcus lanceolatus four times, and the streptococcus pyogenes, the staphylococcus pyogenes aureus, and the bacillus of Friedländer each once; in twenty-three soldiers and servants, the micrococcus lanceolatus four times, the staphylococcus pyogenes aureus six times, the streptococcus pyogenes once, and the Friedländer bacillus once.

Wright[3] isolated from the nasal secretion of ten healthy persons the

[1] Grawitz and Steffen, *Berliner klin. Wochenschr.*, 1894, No. 18.
[2] Von Besser, *Ziegler's Beiträge*, Bd. vi.
[3] Wright, *New York Med. Journ.*, July 27, 1889.

staphylococcus pyogenes albus six times, the aureus and citreus three times, the bacillus lactis aërogenes once, and the micrococcus tetragenus once.

Paulsen[1] made sixty-four cultures from the healthy noses of twenty-seven persons. Eleven of these were sterile, nineteen gave ten colonies or less, sixteen gave up to one hundred colonies, twelve several hundred colonies, and six furnished countless colonies. Cocci were found much oftener than bacilli. Only once did he find the streptococcus pyogenes. Pathogenic bacteria were not observed in any other of the normal cases. Upon cover-slip preparations he noted spirilla, and Weibel has cultivated a comma bacillus from the nose.

Special interest attaches to the presence of capsulated bacilli in the nose, as these are found with great frequency, if not constantly, in ozæna. The ozæna bacillus of Abel[2] resembles closely the Friedländer bacillus, but is believed by him not to be identical with it. Whether or not this bacillus is ever found in the healthy nose is not established. The Friedländer bacillus and the lanceolate coccus have repeatedly been found in the nose, especially in inflammatory conditions. The rhinoscleroma bacillus is a capsulated bacillus much like the Friedländer bacillus, but differing from it by staining with Gram's method. We do not at present possess an entirely satisfactory differentiation of a group of capsulated bacilli to which Friedländer's bacillus, the ozæna bacillus, the rhinoscleroma bacillus, the capsulated bacillus of Pfeiffer, and some others belong.

The diphtheria bacillus is constantly found in fibrinous rhinitis. Various bacteria, especially diplococci, have been found in the secretion of coryza. When this secretion is abundantly poured out, it often happens that cultures from several drops of it contain very few colonies or are sterile.

Straus has recently made the important observation that the tubercle bacillus is often present in the nasal cavities of healthy persons who spend much of their time in proximity to tuberculous patients. He examined for tubercle bacilli the contents of the nasal cavities of those engaged about hospital wards containing consumptives. Twenty-nine such examinations were made by the inoculation of guinea-pigs. In nine cases the guinea-pig developed tuberculosis. Of these nine persons, six were healthy attendants occupied in such work as sweeping the floor and shaking bed-linen, one was a patient with a chronic non-tuberculous ailment, and two were medical students who spent several hours daily in the hospital. None of these individuals presented the slightest evidence of tuberculosis. These observations are even more significant than those of Cornet as to the abundance and wide distribution of tubercle bacilli in the neighborhood of consumptives.

Wurtz and Lermoyez have found that the nasal mucus possesses considerable bactericidal capacity.

Von Besser found bacteria abundantly in the larynx and bronchi of human corpses, but he demonstrated that after death the fluids from the mouth and naso-pharynx may readily penetrate even into the smaller bronchi, and moreover in his cases the lungs and air-passages were dis-

[1] Paulsen, *Centralbl. f. Bakter.*, Bd. viii. p. 344.
[2] Abel, *ibid.*, Bd. xiii. p. 161.

eased; so that he attaches no importance to his observations as bearing upon the question of the presence of bacteria in these parts in health.

Hildebrandt[1] found that culture media inoculated with bits of the lung and of tracheal mucus from recently-killed rabbits usually remained sterile, and he concludes that practically all bacteria which enter with the air are retained in the upper air-passages and do not penetrate below the larynx. This protection, however, has its limits, as when the inspired air was loaded with fungus-spores these could be demonstrated after half an hour in the lungs. That foreign particles in the air may be conveyed into the lungs is evidenced by the coal particles regularly found in the lungs.

Wargunin, in opposition to Hildebrandt, isolated nine different kinds of bacteria from the trachea, bronchi, and lungs of recently-killed healthy animals.

The observations of the writer are in harmony with Hildebrandt's results as to the usual absence of bacteria, at least in sufficient number to be demonstrable by ordinary culture methods, in the bronchi and lungs of healthy animals.

At autopsies on human beings bacteria, including the micrococcus lanceolatus and the streptococcus pyogenes, may be found in the lungs without noticeable lesion of this organ.

The action of the ciliated epithelium and coughing would tend to drive out bacteria which may have entered the trachea and bronchi.

The expired air is free from micro-organisms, except as these may be mechanically detached, as in sneezing or coughing.

We are not informed as to the frequency with which bacteria are present in the healthy tympanic cavity. That bacteria may pass up the Eustachian tube into the middle ear is shown by the presence in otitis media of various micro-organisms often found in the mouth and naso-pharynx, notably the micrococcus lanceolatus, the streptococcus pyogenes, the Friedländer bacillus, and the pyogenic staphylococci. There are of course other paths by which micro-organisms may be carried into the middle ear, as the lymphatic and blood-currents, and in meningitis from the cranial cavity.

Netter found constantly in the middle ear of new-born infants, at autopsy, bacteria, and among these were pathogenic forms to which he attributes the frequent occurrence of middle-ear inflammations in infants. In autopsies upon one hundred and eight infants less than one year old H. Kossel found otitis media in eighty-five cases. The most common organism in these cases was a delicate bacillus, apparently identical with Pfeiffer's pseudo-influenza bacillus (38 cases). In addition were found the diplococcus pneumoniæ (10), streptococci (4), thick bacilli (2), staphylococci (2), and the bacillus pyocyaneus (once). One case was tuberculous otitis. Some writers are of the opinion that changes often found in the middle ear of the new-born are post-mortem alterations.

Stomach and Intestine.—The study of the micro-organisms present in the stomach and intestine presents many points of physiological and pathological interest, but we must confine our attention chiefly to those of surgical interest. When we consider the relations of intestinal bacteria to various surgical affections, such as perforative and

[1] Hildebrandt, *Ziegler's Beiträge*, Bd. ii.

other forms of peritonitis, appendicitis, and even infections remote from the intestinal canal, it is apparent that this subject claims the attention of the surgeon.

The main sources of the micro-organisms of the stomach and intestine are the ingesta and the air. From these sources countless bacteria and fungi of all kinds are introduced into the alimentary canal, but, as is true of other exposed mucous surfaces, only a limited number of species are capable of prolonged existence in this situation.

The meconium of the new-born infant is sterile, but within twenty-four hours after birth it usually contains abundant bacteria. Although many varieties of bacteria may be found, Escherich has demonstrated a constant bacterial flora in the fæces of milk-fed infants. These constantly-present intestinal bacteria are the bacillus lactis aërogenes, predominating in the small intestine, and the bacillus coli communis, predominating in the large intestine. These bacteria remain throughout life as the obligatory and characteristic intestinal bacteria of man in health, and as they are frequent secondary invaders of the body in disease, and may be concerned in various surgical and other diseases, much practical interest attaches to them.

The bacterial flora of the small intestine, particularly in its upper part, is more varied, as tested by plate cultures, than that of the large intestine. In fact, the comparison of the results of microscopical examination and of cultures from the stools indicates that a large number of the bacteria in the fæces are dead.

As there is very little free oxygen in the intestinal canal, the conditions are not favorable for the multiplication of obligatory aërobes. Most of the bacteria found in the intestine are strict anaërobes or facultative anaërobes, but anthrax spores, which require oxygen for their germination, develop into bacilli in the intestinal canal.

It is certain that pathogenic bacteria of many kinds often find their way into the intestinal canal; in fact, there is probably no pathogenic germ which may not in certain individuals and in certain times and places be present in the intestine.

It is true that the acid gastric juice may kill many of the micro-organisms which enter the stomach, but there are many which resist its action. If we were to rely exclusively upon the results of experiments in the test-tube on the germicidal action of the acid gastric juice, particularly the very acid juice of some animals, we should consider this action a formidable obstacle to the passage of living bacteria into the intestine. But when we consider the insusceptibility of many bacteria to weak acids, the relatively slight and varying acidity of the human gastric juice, the absence at times of any acid in the stomach, the withdrawal in large measure from the direct and concentrated action of the gastric juice of bacteria contained in ingested masses of food and large volumes of fluid, and the rapidity with which the gastric contents may pass into the duodenum, we can understand how micro-organisms, even those very susceptible to acids, may find frequent opportunity to enter the intestine. Only a fraction, usually not more than .05 to .1 per cent., of the total acidity of the stomach is due to free hydrochloric acid, and the proteid hydrochlorides possess very little bactericidal power.

Many organisms can grow in the human stomach even when it is very

acid, as has been shown by Gillespie.[1] The number and variety of micro-organisms which have been isolated from the human stomach by Macfadyen, Abelous, Oppler, Gillespie, and others are very great, but it would serve no useful purpose to enumerate them here. The bacillus lactis aërogenes, the bacillus coli communis, and the pyogenic cocci may be specified as having been repeatedly found in the healthy stomach.

The list of pathogenic bacteria which have been found in the intestinal contents is a long one. Many are present only accidentally and as a transient phenomenon. Some are found with such frequency as to merit special notice. In general, the conditions are not favorable for extensive multiplication of most pathogenic micro-organisms in the healthy intestine.

Pyogenic cocci are rarely absent from the intestine. They are often present in such small number as to escape detection, but the great frequency with which these cocci, particularly the streptococcus pyogenes, are found in the exudate of perforative peritonitis, where they can rapidly multiply, shows that they are common inhabitants of the intestine. Gessner found a pathogenic streptococcus, probably identical with the streptococcus pyogenes, in large numbers in the duodenum of six persons out of eighteen examined at autopsy.

The bacillus pyocyaneus and the proteus bacilli are also often present in the intestine. The tetanus bacillus and the bacillus of malignant œdema are regular inhabitants of the intestine of herbivorous animals. The micrococcus lanceolatus has been found repeatedly in the human intestine, likewise the bacillus pyogenes fœtidus. The bacillus aërogenes capsulatus has been found by the writer in the intestine in two cases of perforative peritonitis with production of gas. The occurrence of intestinal actinomycosis and of perityphlitis actinomycotica shows that the actinomyces may find its way into the intestine.

There are various other pathogenic bacteria which have been occasionally found in the intestine, but those which have been mentioned are the ones of chief surgical interest. The specific intestinal infections of typhoid fever, cholera, tuberculosis, and anthrax are not considered here. The amœba dysenteriæ, on account of its relation to abscess of the liver and lungs, deserves mention.

In this connection it may be stated that the bile in the normal bile-ducts and gall-bladder is to be regarded as free from bacteria. Under various conditions, however, the colon bacillus and other bacteria, particularly the pyogenic cocci, often wander into the biliary passages. The writer has found very frequently the colon bacillus in cultures made from the interior of gall-stones. It is not uncommon at autopsies to find the colon bacillus, less frequently pyogenic cocci, particularly streptococci, in the bile without any alteration in the bile or evident lesion to explain the migration of these bacteria.

Contrary to an old idea, the bile has not been found to possess any decided germicidal property, at least as regards most bacteria.

Genito-urinary Tract.—It has been shown by Lustgarten and Mannaberg, Rovsing, Steinschneider with Galewsky, Petit and Wasser-

[1] Gillespie, "The Bacteria of the Stomach," *The Journal of Pathology and Bacteriology*, vol. i. p. 279. Here can be found references to the literature of this subject.

mann, and Hofmeister[1] that the healthy *male urethra* always contains bacteria. These are abundant and varied in the fossa navicularis, and diminish rapidly in number and kind toward the posterior part of the urethra. How far back they extend is not positively known. They were found by Hofmeister as far back as eight centimetres from the external orifice under conditions making it probable that they existed at this point, and were not simply pushed back by the sterilized glass tube which was introduced for the passage of the inoculating wire. Urethral bacteria are usually present in urine voided after sterilization of the meatus and fossa, even in the urine passed toward the end of micturition.

Lustgarten and Mannaberg by microscopical examination of the normal male urethra distinguished ten different kinds of bacteria—namely, four bacilli and six cocci. Among the bacilli was the smegma bacillus, which has already been mentioned in describing the bacteria of the skin (page 254). Among the cocci was a diplococcus which they describe as identical in form and staining reactions with the gonococcus. They isolated in cultures seven species of cocci, white and yellow. Among these cocci was found the staphylococcus pyogenes aureus. They observed that the common urethral saprophytes were incapable of causing ammoniacal fermentation of the urine, and that they died when planted in urine.

Rovsing, in opposition to most other investigators, found in the normal urethra pyogenic and non-pyogenic bacteria capable of fermenting urine and identical with many of the bacteria found in cystitis, so that he concludes that the usual source of the bacteria causing cystitis is from the urethral flora and not from the air bacteria.

Steinschneider describes four species of diplococci, identical with forms previously recognized by Lustgarten and Mannaberg, as occurring in the normal urethra. Of these, a milk-white diplococcus, which was met in 87 per cent. of the eighty-six healthy and gonorrhœal cases examined, is regarded as the most common bacterium of the urethra. Next in frequency is an orange-yellow diplococcus found in 44.2 per cent. of the cases. These two species are stained by Gram's method, and need not be confounded with the gonococcus. Steinschneider isolated from three cases a grayish-white diplococcus, and from one case a lemon-yellow diplococcus, which were decolorized by Gram's stain and which may correspond to Lustgarten's pseudo-gonococci. He concludes that in only 5 per cent. of the cases are diplococci found which are decolorized by Gram.

Petit and Wassermann, whose methods were open to objection, cultivated from the normal urethra of four persons five cocci, six bacilli, two sarcinæ, and two yeast-fungi. They did not find a pseudo-gonococcus.

Hofmeister did not find the normal urethral flora as varied as have some observers. Two species of diplococci—viz. a non-liquefying white or yellow, large coccus and a liquefying, smaller, gray coccus—he regards as regular inhabitants of the urethra. An orange-yellow and an opaque white liquefying diplococcus he isolated, each from two cases. None of these four diplococci from recent cultures were decolorized by Gram, but

[1] Hofmeister, *Fortschritte der Medicin*, 1893, Nos. 16 and 17. References to other articles cited are contained in this article.

he states that he repeatedly found in cover-glass specimens from the urethra diplococci which were decolorized by Gram. Once he found the staphylococcus aureus. The normal urethral flora he considers to be non-pathogenic and incapable of surviving long in the urine, although pathogenic bacteria may accidentally be present in the healthy urethra.

The occurrence of the so-called pseudo-gonococci, as first described by Bumm and Lustgarten and Mannaberg in healthy and diseased urethræ, is of importance in reference to the diagnosis of gonorrhœa by microscopical examination. If all of the well-known points, as to the morphology, staining reactions, and enclosure and arrangement within cells, characterizing the gonococcus be observed, most authorities believe that a mistake in diagnosis is possible only in a very small number of cases, if at all. Undoubtedly a microscopical diagnosis of the gonococcus has been made in some cases upon insufficient evidence, and it must be admitted that a positive microscopical diagnosis is sometimes attended with great difficulties. We now possess methods which enable us without serious practical difficulties to isolate and study the gonococcus in cultures.

It cannot be said that investigations have determined satisfactorily the question as to the relative frequency with which the bacteria of cystitis are derived from the urethra or are introduced from without the body. As the bacillus coli communis or the bacillus lactis aërogenes is one of the most common bacteria in cystitis, the infection may often be from the intestinal canal through the blood-current by way of the kidneys; some believe more directly by continuity or by the lymphatic stream from the rectum. These bacilli are, however, widely distributed outside of the body, and may be present around the genitals.

Although the results of the bacteriological examination of the healthy urine are contradictory, the weight of evidence is decidedly in favor of the view that the urine in the *bladder* in health is free from bacteria, and that if urethral saprophytes, or even some pathogenic germs, gain entrance to the bladder, they do not long survive in a healthy person.

The *female urethra* contains bacteria, and the anatomical conditions are more favorable than in the male for the passage of the urethral bacteria into the bladder. Von Gawronsky in sixty-two cases examined found bacteria in fifteen—namely, the streptococcus pyogenes (3), the staphylococcus aureus (8), staphylococcus albus (1), the bacillus coli communis (2), the bacillus tholöcideum (1). This last bacillus is probably a pathogenic variety of the bacillus lactis aërogenes. It is stated that the urethra in these cases was normal.

The *vagina* contains bacteria in varying number and kind. The cervix and uterus are normally free from bacteria. The absence of bacteria from the uterus is not easily explained, but it has its analogy in the absence of bacteria from various other canals and cavities which communicate with passages containing bacteria, as, for example, from the bladder and the bile-ducts. The factors usually cited in explanation of this important provision of nature are mechanical hinderances to the penetration of bacteria resulting from the anatomical structure of the parts and the germicidal properties of the secretions. The principal emphasis is usually laid upon the latter factor.

The bacterial flora of the normal vagina contains various bacilli and

cocci, which do not grow on our ordinary culture media, but can be recognized by microscopical examination. Doederlein[1] has described a non-pathogenic bacillus or a group of bacilli which he has cultivated upon a specially prepared acid medium, and which are characterized by marked acid fermentation of sugar. These vaginal bacilli are regarded by Doederlein as the only bacteria to be found regularly in the normal vaginal secretion, and upon their presence or absence he has based his distinction between normal and pathological vaginal secretions. It has, however, been shown by Krönig and Menge that Doederlein's bacillus is often absent from the normal vagina, and that it cannot, therefore, serve as a distinguishing character of the normal secretion.

According to Krönig[2] and Menge[3] the regular bacterial inhabitants of the normal vagina are obligatory anaërobes, and can be cultivated only in anaërobic cultures. They do not describe in detail the characters of these vaginal anaërobic bacilli and cocci, but they say that they are non-pathogenic. In microscopical preparations Menge found in the normal vaginal secretion of non-pregnant women bacilli more abundantly than cocci, but the latter were never missed. He found Doederlein's bacilli in the minority of cases, and more frequently short, thick rods and delicate, thin, curved rods.

According to Menge, bacteria capable of cultivation in alkaline aërobic culture media are present abundantly near the outlet of the vagina, but are usually absent, and when present only few, in the upper part of the normal vagina. He found only once out of fifty cases examined a pyogenic coccus. This was the streptococcus pyogenes, which existed as a persistent organism throughout the vaginal canal of a non-pregnant woman with gonorrhœa of the cervix and thin cervical discharge. The reaction of the vaginal secretion was alkaline.

Diplococci similar to those from the urethra already described occur also in the vagina, and what was said in that connection as to pseudo-gonococci applies here. Koplik[4] has isolated from the normal vagina of children a white diplococcus, and from the vaginal discharge in simple, not gonorrhœal, vulvo-vaginitis in children two white diplococci and a yellow diplococcus. None of these were decolorized by Gram's method or need be mistaken for the gonococcus.

The question as to the occurrence of pathogenic organisms in the normal vagina has been and is still a subject of vehement controversy among obstetricians, who are divided into two camps as to the desirability of antiseptic irrigations of the vagina and as to the frequency of so-called auto-infection as a cause of puerperal infections. The question is also of interest to the surgeon in relation to hysterectomy and in general to operations involving the vagina and uterus.

The results of different investigators on this point have been extremely divergent, and, notwithstanding the large amount of work done, it is not possible at present to express a final judgment. Some investigators have found pyogenic bacteria frequently in the vagina of pregnant women. Thus, Steffeck found pus-producing organisms in 41 per

[1] Doederlein, *Das Scheidensekret, u. s. w.*, Leipzig, 1892.
[2] Krönig, *Deutsche med. Wochenschrift*, Oct. 25, 1894.
[3] Menge, *ibid.*, Nov. 15, 22, 29, 1894.
[4] Koplik, *Journal of Cutaneous and Genito-Urinary Diseases*, June and July, 1893.

cent. of the twenty-nine pregnant women examined. Others have failed to find pyogenic bacteria, with the exception of the gonococcus, in all of the cases examined, or have met them only exceptionally. Most of the later investigations in which a proper technique was adopted are in accord as to the infrequency with which pathogenic bacteria, with the exception of the gonococcus, are to be found in the vagina of either pregnant or non-pregnant women.

In a bacteriological examination of one hundred and ninety-five pregnant women Doederlein found in 55.3 per cent. acid normal vaginal secretion, according to his definition. The only bacteria were the acid-producing vaginal bacilli. In 44.6 per cent. of the cases he found what he calls pathological secretion, which was feebly acid, neutral, or alkaline, and contained various bacilli and cocci. The streptococcus pyogenes he found in 9.2 per cent. of the so-called pathological secretions, or in 4.1 per cent. of the one hundred and ninety-five cases examined. To the staphylococci present he attributes no importance in the causation of puerperal fever. The oïdium albicans is often found in the vagina, but is without significance as a cause of primary infection.

Krönig found the vaginal secretion of all the pregnant women (about five hundred) whom he examined to be acid, the intensity of the reaction varying in different cases. The bacterial flora was of the same general character as that already described for the normal vagina. In no case did he find the streptococcus pyogenes or pyogenic staphylococci. His conclusion, that the streptococcus pyogenes and the pyogenic staphylococci are never present in the vagina of pregnant women, and that if they should enter they must of necessity be quickly destroyed, cannot be accepted without discrediting the results of other competent investigators, but we may admit that they are present only exceptionally.

Experiments have been made by Krönig and Menge proving that bacteria, including the streptococcus pyogenes and pyogenic staphylococci, introduced, even in large number, into the vagina of pregnant or non-pregnant women, disappear in a short time. Thus, Krönig found that the bacillus pyocyaneus disappeared from the vagina of pregnant women in from ten to thirty hours, the staphylococci in from six to thirty-six hours, and the streptococcus pyogenes, with which only three experiments were made, within six hours. No difference was observed, as to the rapidity with which these foreign organisms disappeared, between the normal and pathological secretions in Doederlein's sense, including those containing gonococci. Menge found in non-pregnant women that the bacillus pyocyaneus disappeared from the vagina on the average in twenty-one hours, the staphylococcus pyogenes aureus in twenty-six hours, and the streptococcus pyogenes in twenty-two hours. In only one case did the vagina become infected, and this was with the staphylococcus aureus in consequence of an accidental injury to the wall. In the other cases the bacteria immediately after their introduction began to disappear. In most instances an increase in the leucocytes in the vagina was observed.

Menge has attempted to discover the factors concerned in the production of this powerful bactericidal property of the vaginal secretion. He attaches some importance to the acid reaction to which Doederlein had called attention as the essential factor, but this cannot be the sole or

the principal factor, as the vaginal secretion of non-pregnant women, although usually acid, may be alkaline, and the bacteria disappeared about as rapidly from the alkaline as from the acid secretion. We cannot at present give any satisfactory explanation of the bactericidal properties of the vaginal secretion.

Irrigation of the vagina with water or with antiseptics diminished the rapidity with which bacteria introduced into the vagina disappeared.

Bacteria introduced into the cervix uteri likewise disappeared in a short time. The secretion here is alkaline.

As a result of the investigations of numerous observers we may conclude that the normal vagina of pregnant and non-pregnant women may contain pathogenic bacteria. With the exception of the gonococcus, such bacteria are not often present, and the vaginal secretion does not, as a rule, permit the prolonged survival of most of the bacteria, including pathogenic forms, which may enter. Powerful as these normal defences are, they may, however, be overthrown under conditions which we now only imperfectly understand.

Much emphasis has been laid upon the fact that pyogenic cocci occasionally found in the vagina have manifested, with few exceptions, little or no virulence when inoculated into animals. It should, however, be remarked that the same negative result of the animal experiment sometimes follows the inoculation of streptococci cultivated from cases of puerperal infection. The animal experiment is not decisive as to the possibilities of these pyogenic bacteria in man, and it has been proven that pyogenic cocci without virulence for animals may infect human beings.[1]

Bacteria in Woman's Milk.—Serious errors of interpretation of their observations have been made by several investigators of the subject of excretion of bacteria by the milk, by not recognizing the fact that milk obtained from the breasts of healthy women regularly contains bacteria. The milk as secreted by the gland is undoubtedly sterile in health, but bacteria derived from the skin are mingled with the milk. These bacteria gain access to the milk in the lacteal ducts within the nipple. By far the most common of these bacteria is the staphylococcus epidermidis albus, described by investigators of this subject as the staphylococcus pyogenes albus. This coccus is a regular inhabitant of the milk in the lacteal ducts near their outlets. Surprise has been expressed by Honigmann[2] and others that of all the cutaneous bacteria this should be usually the predominant or the only one found in the milk, but it appears to the writer that his investigations as to the behavior of this organism in the skin explains satisfactorily the appearance of this coccus in the milk. Of all the cutaneous bacteria, this is the only one which penetrates regularly into the deeper layers of the epidermis and into the glandular appendages of the skin. Occasionally other bacteria, also derived from the skin, are present in the milk. The staphylococcus pyogenes aureus

[1] A full review of the bacteriological literature of the subject of puerperal auto-infection up to the date of its publication, together with the report of original observations, will be found in a paper by J. Whitridge Williams in *The American Journal of the Medical Sciences*, July, 1893.

[2] Honigmann, *Zeitschrift für Hygiene*, Bd. xiv. p. 207.

has been found in the milk of healthy women in a number of instances.

It is not known how far up the lacteal ducts this normal bacterial flora extends. It is probable that the mammary gland conforms in this matter to the behavior of other glands whose ducts open upon surfaces containing bacteria, and that bacteria in demonstrable number are found only in the excretory ducts near their outlets.

As the staphylococci normally present in the milk have the property of coagulating milk, it can hardly be that any considerable multiplication of these bacteria occurs in the milk within the lacteal ducts. Fokker observed a limited germicidal effect of fresh milk in some cases, but Honigmann in a larger number of experiments with proper technique was unable to determine any such property, even as regards the typhoid and the cholera bacilli, which are readily killed by blood-serum.

Sources of the Bacteria in Surgical Infections.

Internal Sources.—We have learned that pathogenic bacteria, and particularly the pyogenic micrococci, may be present upon the skin and various exposed mucous membranes of healthy human beings. These bacteria are of course derived primarily from external sources, but some of them may live for a long time or indefinitely on exposed surfaces of the body, and are found here so often that it is proper to recognize the patient's own body as one source of the bacteria concerned in surgical infections.

Internal sources of wound-infection are in general less commonly operative and less dangerous than the external sources. One explanation of this is that the pyogenic bacteria commonly found in the healthy body are often less virulent than those derived from many external sources. The streptococcus pyogenes when cultivated from healthy mucous membranes is often of very slight or no virulence, as tested upon animals, although occasionally highly virulent streptococci are found under these circumstances. The pyogenic staphylococci, and particularly the staphylococcus albus, are often of greatly attenuated virulence when isolated from the exposed surfaces of healthy persons. The lanceolate micrococcus is present in a virulent state in the mouths of only about 15 per cent. of healthy persons, although it is oftener present in a non-virulent condition. The bacillus coli communis obtained from healthy fæces is usually of very slight pathogenic power.

There are various influences which may be cited to explain the relatively slight virulence of many of the pathogenic bacteria present in the healthy body. Among the most apparent are the struggle for existence with the regular saprophytic flora of the body, the influence of the products of the latter organisms, and especially the antibacterial properties of the fluids, secretions, and living cells of the body. That under circumstances which we at present little understand the bacteria of the body may acquire unwonted virulence seems certain.

Highly virulent staphylococci and streptococci may be present on the exposed surfaces of the healthy body without doing any harm. The protection of the body from infection with the pathogenic bacteria which it often harbors is due not so much to the lowered virulence of these bac-

teria as to the defences which have been set up against their invasion and to the local and general resistance offered to their growth.

These defences may, however, be overthrown, and under these circumstances pathogenic bacteria originally present on exposed surfaces of the body may cause various local and general diseases. The unsatisfactory term "auto-infection" is sometimes applied to diseases thus produced.

The internal organs and fluids of the healthy body are normally free from bacteria. Bizzozero and Ribbert have found bacteria, often within cells, regularly in the lymph-follicles of the normal rabbit's cæcum, and Bizzozero has found spirilla often in the epithelial cells lining the necks of the gastric tubules in dogs. These are the only examples known of the presence of bacteria in the living cells of the perfectly healthy body, and here the bacteria have penetrated only a short distance beneath the free surface.

It is probable that pathogenic as well as other bacteria occasionally get into the tissues and circulation of healthy persons without doing any harm. It is claimed by some that the invasion of bacteria into the healthy body is not uncommon, and this doctrine is called latent microbism by some French writers. The occasional occurrence of suppuration in a simple fracture of bone or in other injured parts remote from an exposed surface is best explained, at least in many cases, by the lodgement of pyogenic bacteria which have been carried from an exposed surface to the part by the blood or lymphatic current, and which presumably would have done no harm without the presence of a locus minoris resistentiæ. The infrequency of this event, however, indicates that the presence of pathogenic bacteria in the internal organs and fluids of the healthy body is exceptional.

Can a wound become infected by bacteria conveyed to it by the circulating blood? This may happen in individuals already infected, although, even when it is certain that pyogenic cocci are present in the circulating blood, a wound may heal without suppuration. The possibility of the infection of a wound in a previously uninfected person by bacteria conveyed by the blood-current cannot be denied, but we possess no stringent proof of such an occurrence, and all experience goes to show that wound-infection from this source must be very exceptional, if it occurs at all.

With proper technique the surgeon has, as a rule, little to fear from the bacteria of the patient's skin as a source of infection of operative wounds. The only bacterium of the skin which is not usually destroyed by thorough disinfection of the surface is the staphylococcus epidermidis albus, which lies often deeper than can be reached by any of the practicable methods of cutaneous disinfection. This coccus is found with great frequency in wounds treated aseptically or antiseptically, but ordinarily it does not interfere with the process of repair. Under certain circumstances, particularly when foreign bodies are introduced into the wound or when there is strangulated tissue in the wound, it may cause rise of temperature and suppuration. It is the most common cause of stitch-abscesses. It is often associated with other bacteria in suppuration of external wounds and in inflammations involving the skin. It is identical with, or simply a variety of, the staphylococcus pyogenes albus,

but for reasons which have been stated the latter name seems inappropriate for this ordinary, harmless skin coccus. This white staphylococcus is a widely-distributed organism, and it may enter a wound from without as well as directly from the surface of the body.

The source of the bacillus pyocyaneus in wounds is often from the skin of the patient, but this is a widely-distributed organism, and it may also enter from without.

The mucous membranes which normally harbor bacteria on their surface cannot be completely disinfected by any practicable methods, although it is possible to reduce the number of bacteria, in some situations more readily than in others. The utility of attempting before operation disinfection of a mucous surface—as, for example, in operations involving the conjunctiva, mouth, rectum, and the lower genito-urinary tract—must be determined by experience, and on this point the views of surgeons are not in harmony.

Bacteria cannot be completely kept out of wounds of exposed mucous membranes. The kinds of bacteria in the patient's body which are likely to enter such wounds and the special conditions relating to the bacterial flora of the different mucous membranes have already been described. Although wounds involving such mucous membranes as those of the mouth and intestine, which contain vast numbers of bacteria, including often pyogenic varieties, often heal satisfactorily, and even by first intention, the surgeon has no such guarantee of securing primary union as in operative wounds through the skin. The fact that these wounds often heal quickly and without suppuration demonstrates that the mere presence of certain bacteria, even in large number, in a wound does not necessarily interfere with healing. It also supports the view already advocated that the pyogenic cocci often present on certain exposed mucous surfaces are usually of weakened virulence. But the main factor is, after all, the vital resistance of the living tissues to bacteria, including many virulent species.

The pathogenic bacteria often present on the exposed surfaces of the healthy body are, however, of surgical interest, not so much as a source of primary wound-infection, but rather as the specific agents of infection in various local and general surgical diseases. As examples of local diseases of this category may be cited otitis media, appendicitis, perforative and other forms of peritonitis, some cases of cystitis, and certain abscesses. The pneumonias, localized abscesses, pyæmia, and septicæmia which are such frequent complications of diphtheria and certain general diseases, as typhoid fever and other infectious fevers, are due in many instances to the secondary invasion of pathogenic bacteria, particularly pyogenic cocci, normally present on mucous membranes. It is chiefly from the mouth, tonsils, pharynx, and intestine that these invaders enter the body. The primary disease is often one which is attended by some lesion of the mucous membrane which opens the way for the passage of the micro-organism. But it is not enough for the gate to be thrown open. The defenders within must be overcome. Hence it is particularly in conditions where the vital powers of resistance are lowered that we meet with affections caused by the invasion of pyogenic bacteria from the exposed surfaces of the body. That under these conditions, as

well as under others, attenuated bacteria of the body may become exalted in virulence is highly probable.

The term "auto-infection" is associated particularly with the discussions on the causation of puerperal fever. The bacteriological data entering into this discussion have been given in describing the bacteria of the vagina. The evidence is contradictory, but on the whole is opposed to recognizing so-called auto-infection as a cause of puerperal fever, save in a small proportion of cases.

The bacteria most often found in cystitis are such as might readily gain entrance at times to the healthy urethra, but in most cases of this disease, as in so many others, an essential etiological factor is some primary damage to the part, which permits the survival and growth of the invading micro-organisms.

The most common secondary invader of the body is the bacillus coli communis. The first observations of the general invasion of the internal organs of the body by the colon bacillus were made by the writer and reported in May, 1890. We have found in 40 per cent. of the autopsies at the Johns Hopkins Hospital the colon bacillus in one or more of the internal organs, those most frequently invaded being the lungs, kidneys, liver, mesenteric glands, and gall-bladder. In the great majority of these cases the colon bacilli were present without any organic lesion which could be referred to them. Intestinal lesions were found in 75 per cent. of our post-mortem cases of invasion of the colon bacillus. Very little importance is to be attached to the demonstration of this bacillus in internal organs of the body at autopsies in cases without any lesion which can be referred to it.

The fact that the colon bacillus is found with great frequency in internal organs of the body after death from all sorts of causes, and without doing any manifest injury, necessitates caution in the interpretation of cases where its presence is associated with definite lesions. That in some of the cases reported as infections by this bacillus its presence was only that of an accidental, secondary invader seems to the writer certain. There can be no doubt, however, that under certain conditions the colon bacillus may be pathogenic. It is prone to settle in parts already damaged either by some other micro-organism or by some non-infectious agent. In forty-eight cases of acute inflammation, of various kinds and situations, in which we found the colon bacillus, it was the sole organism present in only fourteen. In the majority of cases of appendicitis and of perforative peritonitis we have found associated with the colon bacillus other bacteria, and particularly the ordinary pyogenic cocci. There is reason to believe that the highly resistant colon bacillus may survive in an inflamed part after the primary organism which started the trouble has died out or has been crowded out by the invader.

The colon bacillus has been repeatedly observed alone or in combination with other bacteria in wounds. That it may be the primary infectious agent in various surgical and other inflammations in different parts of the body is established by numerous observations.

The bacillus lactis aërogenes, which most investigators no longer attempt to separate sharply from the bacillus coli communis, is likewise a common invader from the intestinal tract under conditions similar to those relating to the colon bacillus and with similar pathogenic effects.

The streptococcus pyogenes is a far more important cause of surgical infections than is the colon bacillus. It is more commonly present than other pyogenic cocci in appendicitis, peritonitis, and other inflammations of serous membranes, and in septic infections secondary to other diseases. It is a frequent cause of secondary inflammations in the lungs, serous membranes, and other parts, and of general septicæmia in diphtheria, tuberculosis, scarlet fever, typhoid fever, and other infectious fevers, and also in many non-infectious diseases. The source of these various secondary streptococcus infections is often from the mouth, tonsils, throat, and intestine, parts which in their normal condition often harbor streptococci.

Of other bacteria more or less frequently present on exposed surfaces in health, and concerned in various surgical infections, may be especially mentioned the staphylococcus aureus and albus, the micrococcus lanceolatus, the bacillus pyocyaneus, the micrococcus tetragenus, bacillus proteus, and the bacillus of Friedländer.

External Sources.—Bacteria derived from without the body are those chiefly concerned in infections of wounds and most other primary surgical infections. Abundant experience has demonstrated that if all pathogenic bacteria from external sources, as well as those which may happen to be upon the surface of the skin, be kept out of an external wound, no suppuration of the wound occurs.

There are two ways by which external bacteria may enter a wound: one is by contact with objects contaminated with bacteria; the other is by the air. Strictly speaking, air infection is also contact infection, but the distinction implied in the customary use of these terms is a useful one. Experimental and clinical observations have shown conclusively that contact infection is far more dangerous and common than air infection.

The main emphasis of modern surgical technique is laid upon the sterilization of all objects, such as instruments, ligatures, dressings, and the hands of operator and assistants, which are brought into contact with the wound. The principal sources of contact infection of wounds, as enumerated by Park,[1] are the skin and hair, instruments, sponges or their substitutes, suture material, the hands of the surgeon and his assistants, drainage materials, dressing materials, miscellaneous—*e. g.* drops of perspiration, an unclean irrigator-nozzle, the nail-brush, the clothing of the operator or the bystanders, etc. Of these objects the most difficult to disinfect is the skin. We have already considered this subject, so far as it belongs to this article, in describing the bacteria of the skin.

The pyogenic cocci, which are the bacteria concerned in the great majority of cases of wound-infection, are ubiquitous, and it would be useless to attempt to specify all the objects upon which they have been found. The source from which these cocci are derived is not, however, a matter of indifference. The pyogenic cocci, and particularly the streptococcus, derived from infected persons, as from a case of erysipelas or peritonitis or septicæmia, are more likely to cause serious infection of wounds than cocci of the same species derived from other sources.

Of other bacteria sometimes concerned in wound-infection, the bacillus coli communis not only is a constant inhabitant of the normal intestine,

[1] Roswell Park, "Wound-infection," *American Journal of the Medical Sciences*, Nov., 1891.

but is widely distributed in external nature, and the bacillus pyocyaneus, often present on the healthy skin, is likewise a widely-distributed organism. The bacillus pyocyaneus is a comparatively harmless organism in external wounds, but it is capable of exerting serious pathogenic activity, especially in infections from the intestine. The soil is the natural home of the tetanus bacillus, which is abundant in certain localities and rare in other places. It has been found with especial frequency in garden earth and about stables. It is present very commonly in the fæces of herbivorous animals, as has already been mentioned. Sormani observed that tetanogenic material introduced into the alimentary canal of dogs, which subsequently were prevented from receiving additional tetanus bacilli, could be demonstrated as long as sixteen days after its reception. The bacillus of malignant œdema is likewise a common inhabitant of the soil. In infected localities the anthrax bacillus lives in the soil. In fact, the upper layers of the soil are the great home of bacteria of all sorts, and pyogenic cocci have been found in this situation. The proteus bacillus, which is capable of assuming pathogenic activity, is commonly found in decomposing animal substances.

Flies and other insects may be the carriers of all sorts of infectious agents. Pyogenic staphylococci have been found in the excrements of flies, and even the susceptible cholera bacillus passes unharmed through the alimentary canal of flies.

Certain surgical infections are associated particularly with injuries from definite objects, as, for example, necrogenic warts, containing tubercle bacilli, from cadavers; zoonotic erysipeloid from crabs and other shellfish; oyster-shucker's keratitis; actinomycosis from oats and other grains; anthrax from hides, wool-sorting, and other handling of material from infected animals.

It has been demonstrated by La Garde[1] that bullets obtained from previously unopened boxes as sent out by the manufacturer are practically sterile, but that if the bullets become contaminated with pathogenic bacteria, the latter are not destroyed in the discharge and transit of the bullet, and are capable of infecting wounds. He was able to infect rabbits with the streptococcus pyogenes and other pathogenic bacteria by firing infected bullets through the ear.

As compared with contact infection, infection of wounds from the air is of minor importance, but surgeons are not agreed as to whether or not the dangers of air infection are so slight under ordinary conditions that they need not be taken into consideration at all. In the early days of antiseptic surgery bacteria of the air were thought to be frequent agents of wound-infection and the carbolic spray was introduced by Lister with the intention of destroying them. There followed a period when surgeons considered that the air bacteria could be wholly neglected as a source of traumatic infection, and this is probably still the opinion of the majority of surgeons. At present there is a tendency again to pay more attention to the possibilities of infection from this source, and some surgeons have even gone back to the use of the spray.

Bacteria are always present in the air over the ground and around human habitations, whereas sea-air at a considerable distance from land

[1] La Garde, *New York Medical Journal*, Oct. 22, 1892.

and the air at high altitudes is nearly or quite free from micro-organisms. Bacteria do not usually occur in the air as single, detached cells, but rather as clumps attached to particles of dust, so that in a perfectly quiet atmosphere, as in a closed room, these particles containing bacteria rapidly settle upon underlying objects. Bacteria, being thus attached to particles of dust, are readily filtered out from the air by passing it through porous substances, such as cotton-wool. The bacteria are carried down by drops of rain, and the air of a room may be freed from floating bacteria by producing an artificial rain by some form of douche or spray apparatus.

Whatever creates dust, such as the entrance or exit of a body of students, and other movements in a room, brings bacteria into the air.

It is a fact of fundamental hygienic importance that fine particles, including bacteria, are not detached from moist surfaces even by strong currents of air. Hence comes the hygienic value of using moist cloths in removing dust and in cleansing a room. Substances containing infected material should not be allowed to dry under conditions in which dust therefrom can be conveyed into the air. In the present era of dry dressings for wounds there is frequent opportunity for the scattering of dust from the discharges dried on the dressings in the removal and subsequent handling of these dressings, unless especial care be taken to prevent this in all cases where pathogenic bacteria may be present.

The number of bacteria in the air varies greatly under different conditions. In general it may be said that living micro-organisms are less abundant in the air than was formerly supposed. They cannot multiply in the air, and only those whose vitality is not destroyed by drying can exist in the air. Desiccation may lessen the virulence of pathogenic bacteria without actually destroying them.

What interests us chiefly in this connection is to know whether pathogenic bacteria, and more particularly the pyogenic cocci, occur in the air, and, if so, how frequently and under what conditions.

Pyogenic staphylococci and streptococci have been repeatedly found in the air, although generally only in small number. Obtained from this source, these cocci are often of only slight virulence, but highly virulent staphylococci and streptococci have been isolated from the air. Among those who have isolated pyogenic cocci from the air may be especially mentioned von Eiselsberg, Emmerich, Neumann, Prudden, Ullmann, Haegler, C. Fraenkel. Haegler[1] demonstrated that streptococci may preserve their vitality and power of development for at least thirty-six days, and staphylococci for one hundred days, in pus dried on bandages.

Pyogenic staphylococci and streptococci have been found far more frequently in hospital wards and operating amphitheatres than elsewhere. Haegler found staphylococci and streptococci in the majority of his examinations of the air in the wards and operating-rooms of the hospital in Basle, and the number of such cocci present was in general proportionate to the opportunity for entrance into the air of cocci from dry material and to the amount of stirring up of dust by movement in the room. He also detected in a number of instances the bacillus pyo-

[1] Haegler, *Beiträge zur klinischen Chirurgie*, Bd. ix. p. 496.

cyaneus in the air. Streptococci have been found frequently in the air of rooms containing cases of erysipelas.

Haegler found the pyogenic cocci on the hair and coats of surgeons, and in cobwebs in hospital rooms, as well as on other objects. He concludes from his investigations that the danger of infection from the air is greater than is assumed by many surgeons.

Schimmelbusch and some other investigators have found pyogenic cocci very rarely in surgical wards and operating-rooms. It is sufficiently apparent that various circumstances, such as the care exercised in the destruction or sterilization of material infected with discharges, the use of disinfectants, the isolation of infected cases, and the observance of strict cleanliness, must influence the results of these examinations of the air of hospitals, and that the danger of air infection may be considerable in one place and reduced to a minimum in others.

Air infection may readily become contact infection by bacteria from the air being deposited upon the hands of the operator or his assistants, upon instruments, dressings, or other objects which are brought into contact with the wound.

Micro-organisms which are capable of development only within the living body are called obligatory parasites. A facultative parasite is one whose ordinary mode of life is saprophytic, but which is capable of a parasitic existence, and a facultative saprophyte is one whose ordinary existence is parasitic, but which can grow outside of a living host. These distinctions, however, cannot always be sharply carried out in practice. Although we can cultivate the gonococcus outside of the body in specially prepared artificial media, there is no reason to suppose that it multiplies, or even long survives, in the outer world under ordinary conditions, and immediate contact with the infected person is the principal source of infection. The tubercle bacillus also can be cultivated artificially, but conditions must be exceptional which permit its multiplication outside of the body. Unlike the gonococcus, the tubercle bacillus is capable of prolonged survival outside of the body, and, as is well known, it is a widely-distributed organism. The leprosy bacillus has not been cultivated artificially, and it is ranked among the obligatory parasites. Intimate contact with an infected person seems to be the usual source of infection, although opinions are divided as to the mode of transmission of this disease. The micro-organisms causing syphilis and hydrophobia are unknown, but they are doubtless obligatory parasites.

The bacteria causing anthrax, tetanus, malignant œdema, and actinomycosis are facultative parasites. The pyogenic cocci find the best conditions for their multiplication in the living body or material rich in organic matter, but these ubiquitous bacteria can often find natural opportunity for multiplication outside of the body.

The only bacteria infectious for human beings which are positively known to develop spores are the bacilli of tetanus, anthrax, and malignant œdema, all killed by exposure in a moist condition for a few minutes to boiling temperature. It is generally stated that the tubercle bacillus forms spores, but this is not positively demonstrated. There is still greater doubt as to the formation of spores by the bacilli of glanders, typhoid fever, and leprosy. The tubercle bacillus, the pyogenic

cocci, and the typhoid bacillus are among the more resistant bacteria which are not proven to form spores.

Portals of Entry of Bacteria in Surgical Infections.

The portals of entry or atria of infection are the skin and the exposed mucous membranes of the respiratory, alimentary, and genito-urinary tract, and wounds of these surfaces. The fœtus may become infected either by germinal, or far more frequently by placental, transmission of infectious micro-organisms. In our laboratory experiments we rarely imitate the precise conditions of natural infection, but we make frequent use of methods of inoculation which occur only exceptionally or not at all under natural conditions, such as the injection of bacteria directly into the vessels, into the serous cavities, and beneath the skin, and forced inhalations of large numbers of micro-organisms.

Most of the bacteria concerned in surgical infections are capable of entrance through any portal and of producing infection in any part of the body, but there are some which are restricted to certain modes of entrance and to certain parts of the body. Examples of the latter group are the bacteria causing gonorrhœa and tetanus.

Let us consider briefly the defensive arrangements which exist normally at the various portals of entry. These are partly mechanical, and due to the anatomical structure of the part. The thick epidermal covering of the skin and orifices of the body is impenetrable to most bacteria. The thick layer of laminated flat epithelium covering the mucous membranes of the mouth, œsophagus, and vagina is a hardly less efficient mechanical protection. The more delicate mucous membranes covered by cylindrical epithelium are so situated as to be less exposed to injury, but even these surfaces do not ordinarily permit the penetration of bacteria without the occurrence of some damage to their integrity. The ciliated epithelium of the respiratory tract drives foreign particles toward the natural outlets. The tortuous arrangement of the upper air-passages filters out most of the bacteria which are inhaled. Bacteria which may happen to enter the bladder or uterus or the glandular ducts, such as the salivary, biliary, or pancreatic, which are normally free from bacteria, would be likely to be discharged with the secretions. Obstruction of these ducts predisposes to their infection.

There are certain situations, particularly the tonsils and the lymphatic follicles of the intestine, which, by the delicate nature of their covering, are especially exposed to the invasion of bacteria. These are vulnerable parts, as is shown by the frequency with which primary and secondary infections start from them, but there is reason to believe that the lymphatic tissue in these situations is richly endowed with vital properties hostile to the development of bacteria.

Of equal importance with these mechanical defences are the antibacterial properties of the secretions on mucous membranes. These properties depend partly on the chemical reaction (gastric juice, vaginal secretion), partly on the antagonism offered to invaders by the regular bacterial flora of the surface, but mainly upon bactericidal qualities at present little understood as to their cause, but unquestionable as to their existence.

Micro-organisms find at the gates of entrance living cells and fluids which in health are capable of destroying many of them, and if they pass these gates, it is usually only to be arrested and destroyed at the nearest lymphatic glands. Nor are these protective agencies limited to the lymphatics or to any particular organs: they are present in the blood and everywhere throughout the living body, although more highly developed in some places than in others. Whether the battle against the invaders be within the cells, as is assumed in the phagocytic theory, or outside of the cells, the weapons of attack must be furnished by the cells. The living body is amply protected in health against all ordinary bacteria which may seek entrance, and the study of the etiology of infectious diseases involves the consideration not only of the characters of the specific agents of infection, but also of the ways in which the natural defences of the body have been overcome. There are infectious micro-organisms to which the healthiest and strongest body is able to offer no resistance, and there are other micro-organisms which are capable of doing harm only when the vital resistance of the body has been lowered.

Can micro-organisms penetrate the intact skin or mucous membranes, or must there always be some pathological change or lesion of continuity of these parts to permit their entrance? This question has been variously answered, but, at least as far as certain membranes and certain micro-organisms are concerned, the evidence must be regarded as conclusive for the affirmative answer. It cannot be doubted that the infectious agents causing malaria, relapsing fever, and the eruptive fevers may enter the body without any defect in the skin or mucous membranes, but our concern is not with this class of diseases.

Garré,[1] in 1885, was the first to make a self-sacrificing experiment which has since been repeated with similar result by several others. He rubbed into the skin of his forearm, in the same way as one would rub in an ointment, a large quantity of a virulent culture of the staphylococcus pyogenes aureus. The skin was left intact. After six hours a prickling sensation, associated with redness and turgescence, developed, and in a few hours more about twenty pustules, each developing about a lanugo hair, had formed. In the course of four days an extensive carbuncle, which discharged pus through seventeen openings, formed, and the axillary glands were swollen.

The largest number of experiments of this character have been by Wasmuth.[2] The experiment succeeds almost invariably when virulent staphylococci are thoroughly rubbed into the human skin, but fails almost constantly to give a positive result upon the skin of animals (rabbits, guinea-pigs). The failure with animals is not due to greater impenetrability of their skin to bacteria, for anthrax bacilli and some other pathogenic bacteria when rubbed into the skin of animals are capable of causing infection. Animals are less susceptible than man to these pyogenic cocci—a fact which should not be lost sight of in drawing inferences applicable to man from experiments upon animals with these organisms. Büdinger has shown that pyogenic cocci nearly devoid of virulence for animals may produce abscesses when rubbed into the human skin.

[1] Garré, *Fortschritte der Medicin*, Bd. iii. p. 165, 1885.
[2] Wasmuth, *Centralblatt für Bacteriologie*, Bd. xii. pp. 824 and 846, 1892.

The mere application of the bacteria to the surface of the skin produces no infection either in man or animals. The bacteria must be well rubbed in or pressed in to cause infection.

Through what channels do the bacteria penetrate the skin in these experiments? There are three possibilities—namely, through the epidermis into the rete Malpighii, into the sweat-glands, or into the hair-follicles and sebaceous glands. Schimmelbusch, Machnoff, and Wasmuth have demonstrated that they enter by way of the hair-follicles, and the last-named author considers that they can enter the intact skin in no other way. He finds a principal support for this view in the fact that he was unable to produce any effect by rubbing the cultures into the skin of the ball of the thumb, where there are no hair-follicles, and in the actual demonstration by himself and previous experimenters of the bacteria in the hair-follicles. This conclusion is in accord with the clinical fact that furuncles form almost exclusively in parts of the skin provided with hairs and sebaceous glands, and often begin as pustules around the hairs.

The objection may be raised that these experiments do not actually prove the possibility of infectious agents penetrating the intact skin, as microscopical lesions may be caused by the rubbing or the pressure. Macroscopical and microscopical examinations, however, failed to show any lesion of the epidermis. Still, a microscopical defect might be difficult to detect, and Schimmelbusch considers it possible that in these experiments a minute breach of continuity may be produced.

As experiments upon rabbits with bacilli of anthrax and of rabbit septicæmia have shown, general as well as local infection may follow the rubbing of certain pathogenic bacteria into the skin. These experiments simply show that certain pathogenic organisms are capable of settling in the healthy skin and causing local infections, which may, however, be the starting-point of general infections. They do not show that microorganisms can pass through the healthy skin and thence invade the body without producing any damage at the point of entrance. It is a well-known clinical fact that in wounds this local damage may be very slight and readily overlooked. Indeed, there is a certain antagonism between the extent of the local infection at the point of invasion and the likelihood of general infection.

We have no conclusive experimental evidence that bacteria can enter the circulation through an intact mucous membrane without causing any lesion whatever at their point of entry. There are, however, many examples of pathogenic bacteria which are capable of attacking a healthy mucous membrane and of producing local and general infection through this channel. The lesion of the mucous membrane in some of these cases may be slight and not readily demonstrable. The gonococcus is certainly capable of infecting an intact mucous membrane. A large number of infectious diseases can be produced by feeding cultures or material containing certain pathogenic bacteria. Examples of such intestinal infections are tuberculosis, anthrax, typhoid fever, Asiatic cholera, hog cholera, and chicken cholera. As has already been mentioned, the points in the alimentary canal most vulnerable to infection are the tonsils and the lymphatic follicles.

As is well known, indifferent foreign particles, such as coal-dust, may

be taken up from the air-cells of the lungs and conveyed by the lymphatic current to the bronchial lymphatic glands, but under normal conditions these particles do not enter the general circulation. It is probable that bacteria may be disposed of in the same way. It is said that some of the bacteria of the septicæmias of animals—as, for example, the bacillus of rabbit septicæmia—may enter the circulation through the lungs without leaving behind any manifest lesion. We have no conclusive evidence that the micrococcus lanceolatus, the streptococcus pyogenes, or the other pyogenic bacteria can pass through the intact lungs into the general circulation without causing some inflammation of the lungs.

The lungs possess the power of disposing of many pathogenic bacteria which have been introduced into them. There have been many experiments made to determine the possibility of infection with anthrax bacilli by way of the lungs, and the conclusions drawn from them have been widely divergent. Buchner and his pupils claim to have succeeded, but Baumgarten and his co-workers reached a different conclusion. Gramatschikoff finds that the intratracheal injection of anthrax bacilli or spores is incapable of causing infection if infection through the wound be avoided. The bacilli quickly perished in the lungs, sections showing degenerated bacilli within four to ten hours.

No infection of an intact mucous membrane, either in man or animals, has been produced experimentally by the mere application to the surface of the membrane of the pyogenic cocci, although there is clinical evidence of the possibility of such a mode of infection.

The chief surgical interest of the question of the permeability of intact mucous membranes to bacteria relates to the explanation of tuberculosis of internal parts without tubercular lesion at any portal of entry, and to cases of osteomyelitis, internal abscesses, and, in general, the cases of so-called cryptogenetic septicæmia and pyæmia, in which the most careful examination fails to detect any point where the bacteria could have entered.

Most authorities are of the opinion that tubercle bacilli can pass through a mucous surface without leaving any trace behind of their presence at the point of entrance. The main support for this doctrine of the passage of tubercle bacilli through intact mucous membranes is found in the clinical facts. Orth and Wesener, however, claim that occasionally animals fed with tubercle bacilli develop tuberculosis of the mesenteric glands without any tubercular alteration of the intestinal mucous membrane. Baumgarten contests this, and holds that in all cases of experimental tuberculosis there is a tuberculous lesion at the point of entry. He explains the cases of tuberculosis of lymphatic glands, of bone, and of other parts observed not infrequently in man without tuberculosis of the lungs or any exposed surface by assuming that they are all instances of inheritance of tubercle bacilli. This well-known doctrine of Baumgarten involves also the assumption that tubercle bacilli may remain for an indefinite time alive within the body in a latent condition.

In the opinion of the writer the evidence is in favor of the view that tubercle bacilli may enter the lymphatic circulation without causing any tuberculous affection at the point of entrance. In many cases, however, where this explanation might at first be thought to be the correct one,

careful search will reveal the atrium morbi, not infrequently in the form of a small healed tuberculous focus in the lungs or other exposed part. H. P. Loomis has found tubercle bacilli in the bronchial glands without tuberculous lesion in any part of the body.

It is not possible at present either to prove or to disprove, for man, the possibility of the passage through an intact mucous membrane of the pyogenic cocci, which are the organisms usually concerned in the so-called cryptogenetic pyæmic and septic processes. It is true that the most careful examination in many of these cases fails to reveal the atrium of infection, but who can say that it may not have been overlooked? The more painstaking the search, the more likely is some portal of entry to be found. This portal may be the root of a carious tooth, the middle ear, one of the nasal sinuses, or some other part not usually examined at autopsies. Who can feel sure that in the whole vast extent of the alimentary, respiratory, or genito-urinary mucous membranes some minute lesion, serving as a point of entry, does not exist? Such a lesion may be microscopic in size, perhaps no more than a necrotic epithelial cell. Moreover, we have to consider that the original lesion at the point of entry may have healed without leaving any recognizable trace; nor need this lesion be a recent one. There are instances of fatal septicæmia following mere punctures and scratches of the skin which gave rise to scarcely any local inflammation, and the septicæmia may develop after the point of original injury has healed and been forgotten. Bacteria, including pathogenic species, may remain alive, but quiescent, for weeks and months, in some instances it would seem even for years, within the body, and then, as the result of a trauma or some other cause, their pathogenic energies may be stimulated into activity.

While it is certain that in many instances pathogenic micro-organisms may invade an intact mucous membrane and cause local and general infection, and that in some instances the organism may enter the circulation and be transported to distant parts without manifest lesion at the point of entrance, and while the possibility of the latter occurrence cannot be disproven in the case of the pyogenic cocci, nevertheless there can be no doubt that pathological alterations and wounds of the exposed surfaces of the body open the way for the entrance of the pathogenic micro-organisms in most surgical infections. For some pathogenic organisms, including pyogenic cocci of exalted virulence—such as may come from a case of puerperal peritonitis, for example—all that is needed is that the parts should be thus opened, and infection is sure to follow their entrance. But we have only to contrast the frequency with which streptococcus and other pyogenic infections complicate or follow the infectious fevers, such as typhoid, characterized by lesions of mucous membranes, or the frequency with which infection follows external wounds in diabetic and dropsical persons, with the rarity of such a sequel to injuries of the same parts in a healthy person, to appreciate the importance of other factors than the mere breach of continuity in an exposed surface in predisposing to local and general infections. We shall consider later these local and predisposing causes of surgical infections.

Interesting experiments have been made by Schimmelbusch, Nissen, Pfuhl, and others as to the rapidity of absorption of bacteria from fresh

wounds. They have demonstrated that bacteria are taken up within a very short time, by the lymphatic and blood-vessels, from a fresh bleeding wound. Mice inoculated with anthrax bacilli at the tip of the tail died of anthrax in spite of amputation of the tail ten minutes after the inoculation. Nissen found anthrax bacilli in the nearest lymphatic glands within one hour and a half after peripheral inoculation of an extremity. The application to smooth fresh wounds by Schimmelbusch of a moderate quantity of a culture of the anthrax bacillus or of a streptococcus lethal to mice was fatal, notwithstanding an immediate attempt at disinfection of the wound with the strongest antiseptics. Schimmelbusch and Ricker[1] were able to demonstrate in cultures from the internal organs (lung, liver, spleen, kidney) anthrax bacilli in an hour, or even half an hour, after the inoculation of fresh wounds of mice with this organism. They showed that this rapid absorption of bacteria from fresh bleeding wounds applies equally to pathogenic and saprophytic bacteria. In cultures from the internal organs made five minutes after the infection of a fresh wound of a rabbit's thigh with the bacillus pyocyaneus they found many colonies of this bacillus. In making the cultures it is necessary to use the whole organ finely divided.

The significance for the individual of the rapid absorption of bacteria from fresh wounds depends, of course, primarily, upon the character of the bacteria. If these in small or moderate number are capable of causing fatal septicæmia, as is the case with virulent anthrax bacilli in highly susceptible animals, the issue is necessarily fatal; if, as is the case with the pyogenic cocci, the bacteria do not readily gain a foothold where they can multiply, their absorption is of little consequence in most cases, and, so far as the ordinary saprophytes are concerned, their absorption from fresh wounds is a matter of indifference.

The period during which this rapid absorption of bacteria from a fresh wound takes place is of short duration. As soon as a coagulum has formed on the surface of the wound and the open mouths of the lymphatic and blood-vessels are plugged, the conditions are changed, and fine particles like bacteria are no longer quickly transported into the lymphatic and blood circulation. The surface of a healthy granulating wound offers great resistance to the invasion of bacteria, almost as much as an intact exposed surface of the body. Slight injuries, however, such as probing, the removal of dressings, and other manipulations, may convert a granulating surface into a fresh wound, with the accompanying dangers of infection.

Elimination of Bacteria in the Secretions.

In former times it was thought that the body gets rid of infectious agents chiefly by their excretion through the emunctory channels. We now know that micro-organisms are destroyed within the body by the living cells and fluids, and that this method of freeing the body from living bacteria is far more efficient and of much greater importance than that of their excretion by the emunctories.

Pathogenic bacteria often appear in the secretions in various infectious

[1] Schimmelbusch, *Deutsche med. Wochenschrift*, July 12, 1894.

diseases, and it is of interest to know under what conditions they are excreted and in what secretions they occur. The mode of conveyance of infectious organisms from an infected individual to others, and the practical measures of prevention, are determined in large measure by the manner of elimination of these organisms from the infected body.

Wyssokowitsch, as the result of a long series of experiments, came to the conclusion that bacteria in the circulation are never discharged from the body through the healthy organs, but escape only through some breach of continuity or other lesion in the excretory membrane. Hence those pathogenic bacteria which cause some damage to the excretory surfaces—and there are many such bacteria—are most likely to appear in the excreta, although bacteria without this capacity may escape through lesions preformed from other causes.

Not all subsequent investigators of this subject have been able to confirm this law of Wyssokowitsch, and it is true that bacteria may be eliminated from the circulation by way of the excretions without demonstrable lesion of the organ through which they have passed. It is to be remembered, however, that the lesion may be difficult to detect, or may be of some such undemonstrable character as that of the vascular walls in inflammation which permits the passage of leucocytes and red blood-corpuscles.

There have been many special and incidental investigations of the subject of the escape of bacteria with the secretions. Of the experimental investigations relating to the subject in general the most important are those of Wyssokowitsch, Pernice and Scagliosi, and Sherrington.[1]

Sherrington experimented on mice, rabbits, and guinea-pigs by the subcutaneous or intravenous inoculation of eleven, mostly pathogenic, species of bacteria. In sixty-eight observations the presence of the specific micro-organism introduced was detected in the urine twenty-one times; on eight of these twenty-one occasions the presence of blood in the urine was ascertained by the spectroscope; and in a ninth case gross lesions (tubercle) were found in the kidney. Sometimes the urine contained much coagulable albumin. Of the bacteria of surgical importance tested, the staphylococcus aureus, the bacillus pyocyaneus, the bacillus anthracis, and a bacillus probably identical with the Friedländer bacillus were found frequently in the urine. In forty-nine experiments the specific bacilli were found in the bile in eighteen. The bacillus of mouse septicæmia appeared in the conjunctiva, which became inflamed, under conditions making it probable that it did not enter from without. Among the points especially emphasized by Sherrington are the following:

"At a time when every drop of the circulating blood is teeming with micro-organisms there may not be the slightest transit of them into the urinary and biliary fluids then secreted, and they may be completely absent from the aqueous humor of the eye-ball."

"When certain pathogenic species are employed, a number, often very considerable, of the injected bacteria tend after a time to appear in the secretions of the kidney and liver, and their escape in the secreta is

[1] Sherrington, "Experiments on the Escape of Bacteria with the Secretions," *The Journal of Pathology and Bacteriology*, Feb., 1893. This valuable article contains a full review of the literature.

sometimes accompanied by an escape of actual blood," although not infrequently there is no blood in the secreta.

"The evidence is against believing that when this transit of bacteria across the secreting membrane occurs the membrane is still normal in condition, although at the same time it need not be ruptured or pervious to red blood-corpuscles."

"The fact that the escape of the bacteria tends to occur, not immediately upon the introduction of them wholesale into the circulation, but in the late stages of the communicated disease, suggests that the healthy secreting membranes are not pervious to bacteria, and that only after soluble poisons produced by the infection have had time to act upon them do the membranes became pervious to the germs. The fact that species which are innocuous did not in the experiments appear in the secreta at any time is in conformity with this conclusion."

Pernice and Scagliosi experimented with staphylococcus aureus, bacillus prodigiosus, bacillus anthracis, bacillus pyocyaneus, and bacillus subtilis, and they found that these bacteria were constantly excreted through the urine and bile, and might escape through various mucous membranes. This excretion begins six to eight hours after their introduction. Virulent bacteria retain their virulence, as a rule, in the excreta.

There are numerous observations in human beings of the escape of infectious bacteria through the excretions. The pyogenic cocci are particularly prone to settle in the kidney and cause focal inflammations, but even without actual foci of suppuration they often escape into the urine. Nannotti and Baciochi, both in grave suppurative processes and in slight ones, found the specific bacteria with great frequency and of customary virulence in the urine. They disappeared from the urine twenty-four to thirty-six hours after the evacuation of the pus. In experimental pyocyaneus infections the specific bacillus is found regularly in the urine. The micrococcus lanceolatus in pneumonia and other pneumococcus infections, the typhoid bacillus in typhoid fever, the streptococci in erysipelas and other streptococcus infections, are often present in the urine. The bacillus coli communis, the most common of all secondary invaders, often escapes through the kidney.

Pathogenic bacteria are eliminated very often through the bile. One of the most common lesions in various infectious diseases is the presence of focal necroses, sometimes visible to the naked eye and sometimes seen only with the microscope, in the liver, and these permit the passage of bacteria into the bile. It is not, however, necessary that such necroses should be present in order to permit the escape of bacteria into the bile.

Blachstein, in experiments made under the direction of the writer, demonstrated that the colon bacillus and the typhoid bacillus injected into the veins of rabbits often appeared in the bile, where they frequently remained alive and in large number weeks and months after they had disappeared from all of the internal organs. In many of these cases there were focal necroses in the liver. The passage from the circulation into the bile of the anthrax bacillus, of the micrococcus lanceolatus, the streptococcus pyogenes, the pyogenic staphylococci, the bacillus pyocyaneus, and of other bacteria has been repeatedly demonstrated. Patho-

genic bacteria are quite as frequently discharged through the bile as through the urine.

Of course bacteria in the bile will enter the intestine with this secretion, and it is therefore not always easy to determine whether specific pathogenic bacteria found in the intestine in infectious diseases have been discharged through the wall of the intestine or through the liver. Most of the observations recorded concerning the transit of bacteria through the intestinal wall from the circulation have not been made so as to determine whether or not the escape is really through the intestinal mucosa or by way of the bile. Nevertheless, the frequency with which hemorrhages, necroses, inflammations, and ulcers of the intestinal mucous membrane occur in various infectious diseases makes it highly probable that pathogenic bacteria may be eliminated through this channel. Certain it is that the specific infectious bacteria, not only of diseases like typhoid fever, cholera, and tuberculosis, characterized by definite intestinal lesions, but of many other diseases, such as croupous pneumonia, septicæmia, pyæmia, are often found in the fæces.

Tubercle bacilli may be present in the milk of tuberculous cows even when there is no demonstrable tuberculosis of the udder. The statements as to the frequency of this occurrence vary. Ernst demonstrated by the microscope tubercle bacilli in the milk of 28.5 per cent. of the thirty-five tuberculous cows examined, and by inoculation experiments in 50 per cent. of fourteen cows. Bang by the inoculation test found tubercle bacilli in the milk of only nine out of sixty-three tuberculous cows without mammary tuberculosis. When the udder is tuberculous the bacilli are always in the milk.

Numerous observations have been made to determine whether or not the pyogenic cocci are excreted with the milk in puerperal infections, but since we now know that the staphylococcus albus is regularly, and the staphylococcus aureus is sometimes, present in the milk of healthy women, the demonstration of these cocci in the milk in cases of puerperal fever has lost much of its diagnostic significance. There is, however, reason to believe that, although the ordinary source of the staphylococci found in the milk is from the skin, they may be excreted through the gland from the blood in pyogenic infections. The presence of streptococci in the milk is more significant of such excretion than that of staphylococci. In several cases of puerperal fever streptococci have been found in the milk, although more frequently they are missed in this secretion under these circumstances. There is evidence that the pyogenic cocci causing mastitis may enter either from without through the lacteal ducts or may have been deposited from the circulating blood. Karlinski claims to have demonstrated that the staphylococcus aureus injected into the blood of rabbits may be excreted through the mammary gland.

Foà and Bordoni-Uffreduzzi and Bozzolo have found pneumococci in the milk of pregnant women affected with lobar pneumonia, and the former investigators demonstrated their presence in the milk of pregnant rabbits inoculated with this organism, and noted pneumococcus septicæmia in young rabbits which sucked the breast of their infected mothers.

The typhoid bacillus has been found exceptionally in the milk in cases

of typhoid fever. In experimental anthrax the specific bacillus appears in the milk only exceptionally.

Brunner found the staphylococcus albus, von Eiselsberg, Preto, and Tizzoni the staphylococcus aureus, in the sweat in cases of pyæmia. The detection of staphylococci, particularly of the staphylococcus albus, in the human sweat does not necessarily prove that they have been excreted through the sweat-glands from the blood, for even after the most thorough disinfection of the surface of the skin the white staphylococcus has not usually been destroyed in the deeper layers, as has already been explained in describing the bacteria of the skin. Still, it is probable that pyogenic cocci may be eliminated by the sweat-glands, for Brunner has shown that the staphylococcus aureus and the bacillus prodigiosus injected into the circulation of swine can be demonstrated in the sweat from the snout after administration of pilocarpine. He was also able to detect the anthrax bacillus in the sweat from the paw of an infected cat after stimulation of the sciatic nerve. He reports only three experiments, and it is desirable that more work should be done on this subject, as the frequency with which pathogenic bacteria may appear in the sweat in infectious diseases is of importance, especially with reference to possibilities of contagion and to measures of disinfection.

In Brunner's experiment with the bacillus prodigiosus this organism was found also in the saliva, and there are other observations which indicate the possibility of elimination of bacteria through the salivary glands.

Conditions favoring the Development of Surgical Infections.

There are various conditions, relating partly to the micro-organisms concerned and partly to the individual receiving the organisms, which are determining factors in causing infection. The factors pertaining to the individual are usually grouped under the vague but indispensable term "predisposition."

Dosage and Virulence of Infecting Bacteria.—In the case of some pathogenic bacteria a single bacterial cell may be capable of infecting a highly susceptible animal, whereas with a less susceptible animal a large number of the same kind of bacteria may be required. In his interesting studies on the relation of the dosage of bacteria to infection Watson Cheyne[1] showed that whereas a single virulent bacillus of rabbit septicæmia was capable of causing fatal septicæmia in the highly susceptible rabbit, in the less susceptible guinea-pig the fatal dose was 300,000 bacilli and upward; between 10,000 and 300,000 bacilli produced abscesses, and smaller doses were without effect. In a mouse a single bacillus of mouse septicæmia, and in a guinea-pig a single virulent anthrax bacillus, were capable of producing fatal infection, whereas in rabbits and sheep a considerable quantity of the anthrax bacilli was required to kill the animals.

Animals are in general insusceptible to small quantities of the pyogenic cocci, whether introduced subcutaneously or into the circulation. It generally takes several hundred thousand of the cocci to produce local abscesses by intravenous or subcutaneous injection. Man is more susceptible to these cocci.

[1] Watson Cheyne, *The British Medical Journal*, July 31, 1886.

This question of dosage is largely one of individual or racial susceptibility on the one hand, and of virulence of the micro-organisms on the other hand.

The kind of infection produced by some bacteria varies with the dose. It often happens that the inoculation of a very small number of certain pathogenic bacteria produces no effect, a larger number cause only a local abscess, and a still larger number cause fatal septicæmia. This is illustrated by the micrococcus lanceolatus, some varieties of the streptococcus pyogenes, and other pyogenic cocci.

We are familiar with varying degrees of virulence in the case of a large number of pathogenic bacteria. Influences known to be capable of affecting the vitality and the virulence of bacteria, such as sunlight, desiccation, saprophytic growth, association with other bacteria or their products, are widely operative in nature. The virulence of a micro-organism depends probably mainly upon its capacity to form toxic products, as it is by these products that bacteria chiefly produce their pathogenic effects.

Bacteria which enter the body associated with their toxic products are much better adapted to cause infection than when they enter deprived of these products. These toxic substances, by damaging immediately the cells and fluids which protect the body from infection, enable the invader to gain a foothold which it might otherwise not have secured. Vaillard claims that tetanus spores, deprived by heat or by washing of their toxines, are incapable of germinating in the animal body without the aid of accessory causes, such as the presence of other micro-organisms, dirt, other foreign substances, necrotic tissue, although the spores themselves are still alive and in suitable media capable of development. If, however, as is usual in our laboratory experiments, the spores or bacilli be inoculated with the toxin, which in most minute doses is of appalling potency, tetanus is sure to develop. In fact, our experimental tetanus is, as a rule, essentially a pure intoxication.

The varying results which follow the introduction into the body of pyogenic cocci derived from different sources depend doubtless in part upon whether these cocci enter the tissues already equipped with a reserve force of poisonous products or must begin the fight unarmed. The inoculation of infectious material coming directly from the human body, as from a case of puerperal peritonitis, and received perhaps only in a puncture or scratch of the skin, may manifest disastrous effects with which we are not familiar in inoculations with our artificial cultures of the pyogenic cocci obtained from the same source.

The micrococcus lanceolatus, the streptococcus pyogenes, and the pyogenic staphylococci are notable for the wide variations of their virulence. The lanceolate coccus quickly loses its virulence in artificial cultures.

The writer has reported observations as to the varying virulence of the staphylococcus aureus cultivated from different sources. Some broth cultures were fatal to rabbits within twenty-four to forty-eight hours when injected into the circulation in the dose of 0.1 c.c., and other cultures injected in the same way produced no apparent effect in the dose of 1.5 c.c. Between these extremes were cultures of all degrees of intermediate virulence. In the majority of cases 0.2 to 0.3 c.c. of fresh

bouillon cultures killed the animal within three to seven days after intravenous injection. The variations in virulence of the streptococcus pyogenes are even more striking. Pathogenic bacteria, especially pyogenic cocci, obtained from an infected individual are more likely to be highly virulent than when cultivated from other sources. There are, however, many exceptions to this general rule.

In various ways the weakened virulence of pathogenic bacteria may become augmented. Among the most important of those ways with which we are acquainted are repeated passage through the animal body, association with other bacteria or their products, and the addition of certain chemical substances.

The character of the infection varies often with the degree of virulence of the specific micro-organism. Bacterial species, which when highly virulent may kill quickly with septicæmia, may, with weakened virulence, require a much longer period to produce the same effects, or may give rise to only local inflammation without general infection. It is especially with bacteria of attenuated virulence that the matter of dosage may be a controlling factor.

The varying virulence of the pyogenic cocci is one of the factors in the explanation of the remarkably diverse effects which these organisms are capable of producing in the animal body. These cocci may under different circumstances cause all grades and kinds of inflammation, serous, fibrinous, suppurative; they may cause localized inflammations and general infections. But there are other circumstances besides the degree of virulence which control these varying results. Equally important, in many cases more important, controlling factors are the manner of invasion of the micro-organism and various local and general predisposing conditions.

In fact, there is no definite and constant relation between the character and the severity of an infection produced in man by pyogenic cocci and the virulence of the cocci cultivated from the case. From the gravest septicæmias cocci of slight degrees of virulence may be cultivated, and from a simple epidermal pustule cocci of high virulence, as tested upon animals. There is reason to believe that the virulence of the micro-organisms may be modified during the course of an infection, so that we cannot necessarily draw conclusions as to the primary virulence of the organism at the time of its invasion from the virulence noted in cultures from later stages of the disease.

Bacterial Association.—Bacteria are not usually found in the external world under natural conditions in pure culture, but they are mixed together. Mixed infections are common in human beings. In suppurating wounds we usually find more than one bacterial species. It is of importance to learn the relations of these bacterial associations to infection. We are at present only imperfectly informed as to these relations, but we know that they are often of great significance. Only the more salient points which directly bear upon our theme can be considered here.

The association of one bacterial species with another may be without influence upon the development or the properties of either, or one species may be favorable to the growth or enhance the virulence of another, or one species may be antagonistic to another or in various ways modify its

characters. Bacteria exert their influence on each other in large part through their chemical products, and it is often possible to bring about modifications of character by exposing one species to the action of the chemical products of another species.

The pathogenic, the chromogenic, the fermentative, and the other vital manifestations of bacteria may be influenced by their combination with each other. The bacillus pyocyaneus may lose its power of producing pigment when combined with certain other bacteria (Mühsam and Schimmelbusch). In mixed cultures of certain bacteria chemical products may be formed and fermentations produced which neither of the species in the culture is capable of producing by itself alone (Nencki, Burri, and Stutzer). In mixed cultures of two pathogenic bacteria a larger amount of the toxic products of one or both may be formed than either produces when in pure culture (von Schreider).

The effects following the concurrent inoculation of two kinds of bacteria vary. The association may be without influence as regards infection. The result may be that the development of a deadly species of bacterium is checked by the introduction of another species which is relatively harmless. The only striking instance of this is the effect of the inoculation of the streptococcus of erysipelas, the bacillus of Friedländer, and of several other species of bacteria simultaneously with or shortly before or after inoculation with the anthrax bacillus. These bacteria or their products introduced into the body are capable of preventing the developing of the anthrax bacillus and of rescuing the animal from certain death (Emmerich and others). Various explanations of this effect are given by different writers. The effect is probably referable not so much to a direct antagonism of one species to the other as to an augmentation of the antibacterial properties of the cells, which, according to von Dungern and Metschnikoff, is manifested by increased phagocytic activity of the leucocytes. Bacteria in general which cause suppuration may thereby prevent the development of the anthrax bacillus in the focus of suppuration.

More frequently the concurrent inoculation of two species of bacteria increases the danger to the animal from one or both. A combination of two species, each in itself harmless, may prove fatal to the animal (Roger). A bacterium of attenuated virulence may become augmented in virulence by inoculation in combination with another species which need not necessarily be itself pathogenic, or sometimes simply in combination with the chemical products of another species. The following are examples of the exaltation of the virulence or of the pathogenic effects of one kind of bacterium by combined inoculation with another kind or its products: that of the micrococcus lanceolatus by combination with the proteus vulgaris, the anthrax bacillus, or the diphtheria bacillus (Monti, Pane, Mühlmann, Mya); the streptococcus pyogenes with the proteus vulgaris, bacillus prodigiosus, bacillus coli communis (Klein, Monod, and Macaigne); the pyogenic staphylococci with the bacillus prodigiosus or its products and other bacterial products (Grawitz and De Bary and others); the diphtheria bacillus with the streptococcus pyogenes or its products (Roux and Yersin and others); the typhoid bacillus with the streptococcus pyogenes, colon bacillus, and proteus, or their products (Vincent, Sanarelli); the bacillus coli communis with the typhoid bacil-

lus and the streptococcus pyogenes (Pisenti and Bianchi-Mariotti); the bacillus of symptomatic anthrax with the bacillus prodigiosus (Roger). Mention has already been made of the pathological importance of the association of the tetanus bacillus with other bacteria. Of especial interest are the experiments of Prudden demonstrating that the intratracheal injection of cultures of the streptococcus pyogenes in tuberculous rabbits leads to the formation of regular phthisical cavities in the lungs—a result which is not obtained by the inoculation of either microorganism alone. Bernheim has demonstrated that the diphtheria bacillus grows more luxuriantly and with a larger production of toxin in the filtrate of streptococcus bouillon cultures than in ordinary bouillon.

A most important group of infections, many of them of surgical importance, is furnished by the secondary invasion of pathogenic bacteria in the course of various infectious diseases, such as typhoid fever, tuberculosis, diphtheria, scarlet fever, small-pox, and other exanthematous fevers. The streptococcus pyogenes is more frequently the infectious agent in these secondary infections than any other organism, but the other pyogenic cocci are not uncommonly concerned. The primary infection increases susceptibility to these common pyogenic cocci, which often find the way open for their invasion by some lesion of an exposed surface of the body. It is also very probable that the primary infection may bring about conditions which enhance the virulence of the bacteria concerned in the secondary infection. Although it is not necessary to suppose that these common secondary invaders are always derived from those which are present in health upon exposed mucous membranes, nevertheless they doubtless often have this origin. Pyogenic cocci obtained from these secondary infections are usually, although by no means always, more virulent than when cultivated from the healthy mucous membranes.

Of especial frequency and importance among the mixed and secondary infections here in consideration is the association of the tubercle bacillus with the streptococcus pyogenes, the typhoid bacillus with pyogenic cocci, and the diphtheria bacillus with streptococci.

The characters of the various mixed infections are probably determined less by a direct influence of one bacterial species or its products upon another, although this factor appears in some cases to be an important one, than by the action exerted by one or both species upon the resisting powers of the fluids and cells of the body.

Immunity and Predisposition.—In no class of infectious diseases is the influence of predisposition as an etiological factor more apparent than in many of the surgical infections. If a wound could be kept entirely free from pathogenic bacteria, it would not suppurate, no matter how favorable in other respects the local and general conditions for infection might be. The occurrence of suppuration in human beings from sterile chemical irritants is so exceptional that we need not consider this form of suppuration here. It is not, however, possible in all, or even in most, cases to keep bacteria wholly out of a wound. The examination of so-called aseptic wounds shows with great frequency the presence of bacteria, and notably of the white skin-coccus, but also sometimes of other pyogenic cocci, including the staphylococcus aureus. Although the cocci found under these circumstances are usually of weakened viru-

lence, nevertheless, as shown by Büdinger and others, they are of some virulence, and may be decidedly virulent. The frequency with which pyogenic bacteria enter wounds is by no means expressed by the frequency with which wounds suppurate. Every surgeon knows that in certain persons and in certain conditions of the body a wound is much more likely to suppurate than in others, although the same precautions are taken to guard against the entrance of micro-organisms. It is therefore a matter of prime importance, no less of practical than of scientific interest, to learn, so far as we may, what are the conditions which predispose an individual to infection. Unfortunately, we are at present only imperfectly informed as to many of these conditions.

Predisposition is of most importance in the etiology of those infectious diseases which are caused by micro-organisms to which the individual or the species is not in the highest degree susceptible. The pyogenic cocci, in general, belong to this group of micro-organisms, although they may exist in a condition of such exalted virulence that predisposition becomes a factor of no significance.

The degree of susceptibility to a specific micro-organism influences not only the capacity to acquire the infection, but also the course, severity, and character of the infection. In an individual of great susceptibility a micro-organism of attenuated virulence may produce effects which in a relatively insusceptible person can be accomplished only by a highly virulent micro-organism of the same species.

The astonishing variety of affections which may under different circumstances be caused by pyogenic cocci, from a simple epidermal pustule to the gravest septicæmia and pyæmia, from a serous to a suppurative inflammation, are to be explained in part by variations in the local or general susceptibility of the individual, although, as already explained, other factors, such as the degree of virulence of the organism, the manner of invasion, and the number of organisms introduced, are also important. We possess abundant experimental evidence of the fact that in the relatively insusceptible many pathogenic bacteria remain localized, causing inflammation, whereas the same bacteria in the highly susceptible invade the blood and internal organs, causing general septicæmia.

Immunity.—Our comprehension of the nature and importance of predisposition as a factor in the causation of infectious diseases has been facilitated by the increase of our knowledge concerning the factors upon which immunity from the invasion and multiplication of bacteria depends; but our understanding of the nature of immunity is still most incomplete. It is not necessary for our purposes in this connection to enter into a detailed consideration of the various doctrines of immunity, important as are the results of recent investigations upon this subject. It will suffice to state briefly the more important facts and hypotheses so far as they bear upon the question now under consideration.[1]

We distinguish natural or hereditary immunity from acquired immunity. Immunity may be acquired by recovery from an attack of a specific infectious disease, or may be artificially produced by vaccination with the specific micro-organism or its products, or by the injection of the

[1] The following statements concerning immunity are taken chiefly from the fuller article on this subject by the writer in Pepper's *Text-Book of the Theory and Practice of Medicine by American Teachers*, vol. ii., Philadelphia, 1894.

blood-serum or other fluids from individuals rendered artificially immune.

It is certain that the various kinds of immunity do not all depend upon the same causes. The leading theories of immunity may be brought into two classes—one which attributes immunity to the direct and active intervention of the living cells of the body, and the other which explains immunity by the properties of the extra-cellular fluids. In the last analysis these properties of the body fluids must depend upon the activities of cells, so that we must have recourse either directly or indirectly to cellular functions in any adequate explanation of immunity.

The leading representative of the cellular theories is the phagocytic theory, so elaborately and charmingly developed by Metschnikoff. This supposes that immunity depends upon the seizure of invading micro-organisms by amœboid cells, chiefly leucocytes and other mesodermic cells, and the subsequent destruction of these organisms in the interior of the cells. According to this view the leucocytes are charged with the defence of the body and engage in a veritable conflict with the parasites. The significance of inflammation, according to Metschnikoff, is to bring the leucocytes to the seat of danger, to which they are attracted by the positively chemotactic substances furnished by the micro-organisms. Immunity is acquired when the phagocytes have gained tolerance of the poisons of the specific micro-organism and are no longer repelled by them.

There exists in a very large number of cases unquestionably a parallelism between phagocytosis and immunity, but the action of phagocytosis is by no means always apparent. We know that micro-organisms may be destroyed by extra-cellular agencies as well as within the cells, and it is a fair question whether the micro-organisms before their reception by cells have not already been damaged by these other agencies. It is true that Metschnikoff has proven that phagocytes may take up living and virulent bacteria, and that these bacteria may degenerate and die in the interior of cells, but he has not shown that, as a rule, bacteria when taken up by cells have suffered no injury from extra-cellular agencies. We possess direct observations which prove that bacteria introduced into the body may degenerate and die not only within cells, but also outside of them in the humors.

The humoral theories of natural immunity have been based largely upon the demonstration by Nuttall, Buchner, and others of the bactericidal properties of the blood and other fluids of the body. Buchner has given the name of "alexins," and Hankin that of "defensive proteids," to these bactericidal substances. The bactericidal alexins are believed by Kossell and Vaughan to be nucleins or nucleinic acid. Their action is not exerted equally upon all bacteria, and there is often no parallelism between the presence of this bactericidal property in the blood of the normal animal and the insusceptibility of the animal to a given micro-organism. The important observation has been made, however, that as the result of the introduction of certain micro-organisms the body fluids may acquire bactericidal properties as regards the organism introduced.

The search for the origin of the alexins has led to the view that they

are derived directly from the cells, and particularly from the leucocytes. This has led to a partial reconciliation between the phagocytic and the most prominent humoral theories of immunity. The leucocytes and other cells are, indeed, the defenders of the body against intruding micro-organisms. They furnish the alexins, the weapons of attack. Where they accumulate the defensive material is concentrated, but it is not necessary that the bacteria should be actually incorporated in the body of the cells, although the germicidal properties may be more intense within than without the cells. Such is the explanation of natural immunity now adopted by Buchner and many others.

There is a kind of acquired immunity which is not known to have a parallel in forms of natural immunity. This is the so-called antitoxic immunity. Here, as the result of vaccination with the specific micro-organism or its products, the blood and fluids of the immunized animal have acquired the property of neutralizing the poison formed by the specific organism from which the individual has been immunized. The principles of antitoxic immunity have been worked out for the toxic infections, tetanus and diphtheria. The same principle doubtless holds good for acquired immunity from some other diseases, but for how large a number we cannot say. A most important characteristic of this antitoxic immunity is that by successive injections of increasing amounts of the poisonous substances into the animal the antitoxic or immunizing power of the fluids can be augmented to an astounding degree. It is in this way that the antitoxic power of the fluids may be rendered sufficiently high to exert curative effects when injected after the reception of the specific micro-organism or its products. This so-called serum-therapy has thus far been applied with beneficial results only to cases of tetanus and of diphtheria, and, as regards human beings, it is more efficient in diphtheria than in tetanus.

Local Predisposition.—The term "predisposition" is often used in a loose sense to designate all sorts of conditions which increase the chances of infection, or which augment susceptibility to infection, or which influence the localization, duration, character, or severity of infections. A name which is used to refer to conditions belonging to such different categories, having often nothing in common, is of course objectionable, but common usage sanctions the term, and there appears to be no better one under which to include the various points here to be considered.

We distinguish racial and individual predisposition, inherited and acquired predisposition, local and general predisposition.

Instances abound of differences in susceptibility to infectious diseases between different species of animals, and there are differences also between different races of men; but the most important kind of predisposition, as regards those surgical infections which we are here considering, is individual predisposition.

This individual predisposition may be either inherited or acquired. It may pertain only to one part or to certain parts of the body, or it may belong to the body as a whole. We cannot in many instances determine whether the predisposition is local or general, and, indeed, it is often impossible to draw any sharp dividing-line between local and general predisposition.

Local predisposition may be limited to one or more of the portals of entry for micro-organisms, or it may exist at some point within the body, constituting a so-called locus minoris resistentiæ.

We shall consider first predisposing causes of infection at the portals of entry. We shall have in view under this heading more particularly causes which act locally, but it is to be understood that general predisposing factors to be described later may produce local predisposition.

Under the heading of "Inflammation produced by Bacteria" Dr. Councilman in the preceding article has described the influence upon pyogenic infections of many local predisposing factors, such as the character of the tissue invaded, local anæmia, passive hyperæmia, the withdrawal of nerve-impulses from a part, rapidity of absorption, the introduction of chemical bacterial products, the presence of foreign bodies, previous attacks of inflammation; and the reader is referred to Dr. Councilman's article for these points. It has there been made clear that any interference with the integrity of the tissues and of the local blood- and lymph-circulation is likely to render them more susceptible to pyogenic agents, and to influence unfavorably the character and course of a subsequent inflammation. Wounds through a thick layer of adipose tissue or cicatricial tissue or other poorly-vascularized parts are less able to resist the action of pyogenic bacteria than wounds of such vascular parts as the face.

To the predisposing conditions enumerated may be added œdema of the tissues. How important this is may be inferred from the frequency with which erysipelas and suppuration follow so slight an injury as puncture of an œdematous scrotum or leg. Büdinger found that pyogenic cocci so weakened in virulence as to produce no effect when inoculated into the normal ear of a rabbit set up local suppuration when inoculated into an ear rendered hyperæmic and œdematous by temporary application of a rubber band around the root of the ear.

The withdrawal of nerve-impulses from a part may increase its liability to infection. The factors here concerned are various, the most apparent ones being anæsthesia, disturbances in the lymphatic and blood circulation, and nutritive changes. The question as to the existence of special trophic nerves, the interference with whose function predisposes the part to infectious inflammations, has been considered by Dr. Councilman. In a personal communication Dr. Weir Mitchell has kindly favored the writer with the following expression of his views on this point: "I think it true that the withdrawal of nerve-impulses from a part favors infection; that the withdrawal of nerve-influence with partial failure of circulation in some cases of injury still further favors infection; that there is a condition of traumatic nerve-irritation which, probably by its abnormal influence on nutrition, favors infection. A partial injury of a nerve sets up local neuritis and may bring on ulcers of a peculiar character.[1] It seems to me that if we injure a nerve-supply, the changes in muscular and nerve conditions which immediately take place would favor such chemical changes in the tissues as to make them more or less susceptible to infection."

Abnormalities in the secretions on exposed mucous surfaces and in

[1] Interesting examples of such ulcers are here cited by Dr. Mitchell from the forthcoming book of his son, Dr. John H. Mitchell, on *Nerve-injuries and their Remote Results.*

the glands communicating with them may be a local predisposing cause of infection. Obstruction to the outflow of secretions, and the presence of calculi or foreign bodies in cavities or glandular ducts opening upon exposed surfaces are important predisposing causes of infection, as is exemplified by inflammations of the vermiform appendix, renal pelvis, urinary and gall-bladders, urethra, the biliary, pancreatic, and salivary ducts.

In general, all traumatic and pathological lesions of exposed surfaces of the body, such as wounds, hemorrhages, necroses, waxy degeneration, inflammation, ulcers, stricture, strangulation, perforation, increase in greater or less degree the opportunities for the entrance, lodgement, and multiplication of pyogenic and other micro-organisms.

A suppurating surface, however, offers considerable resistance to the growth and invasion into the body of most pathogenic bacteria. Pus is endowed with marked bactericidal properties, both in its corpuscular elements and its fluid constituents, and the opportunities for absorption from a suppurating surface are much less favorable than from a fresh wound. Sestini found that the bacilli of anthrax and of rabbit septicæmia when applied to a suppurating wound of the rabbit's skin produced no infection, although they readily did so when introduced into a fresh wound. The existence of suppuration, however, lowers the general resistance of the body to bacteria.

The various lesions which interrupt the continuity and integrity of the exposed surfaces of the body become most dangerous channels of infection when the general resistance of the body to infectious agents is lowered, as in various infectious fevers and constitutional diseases.

Experiments and clinical observations have been made with reference to the amount of damage to the intestinal coats which is requisite in order to permit the passage of bacteria from the intestinal canal into the peritoneal cavity. Most observers have found the fluid in the sac of a strangulated intestinal hernia free from bacteria in the great majority of cases. Garré found bacteria only once in eight cases; Rovsing did not find them at all in five cases; nor did Ziegler in five cases; Tavel and Lanz obtained a positive result only twice in seventeen cases of intestinal strangulation; in two out of three omental strangulations they found bacteria; Tietze found bacteria in four out of nine cases, with the possibility that in some of the four cases they were accidentally introduced from without. Sanguineous hernial fluids with bloody infiltration of the intestinal coats were observed without the presence of bacteria, and even the fluid in sacs containing necrotic intestine did not always contain bacteria. The presence of fibrinous peritonitis over strangulated intestine does not necessarily involve the presence of bacteria in the exudate, as this form of peritonitis may be caused by the absorption of the chemical products of bacteria from the intestine (chemical peritonitis). Definite relations between the condition of the intestine and the presence of bacteria in the hernial sac were not observed.

For some at present inexplicable reason Boennecken found bacteria in the sacs of all of the eight strangulated hernias which he examined.

Arndt has shown by experiments on rabbits that bacteria may pass through the strangulated intestinal wall without the existence of necrosis of the intestine, and when the condition of the intestine is such that it

quickly returns to the normal state upon relief from the strangulation. The presence of bacteria in the hernial fluid does not necessarily involve the development of peritonitis. The conditions which permit bacteria to wander from the intestine through its wall into the peritoneal cavity have not as yet been made clear. Tietze has shown that the fluid from a hernial sac possesses marked bactericidal power over some intestinal bacteria.[1]

The entrance of the colon bacillus into the circulation is usually, in our experience, associated with some lesion of the intestinal mucosa, although this is not invariably the case. Absorption of pathogenic bacteria, particularly the pyogenic cocci, from the diseased intestinal mucosa is a fruitful source of various infections of internal parts, and many cases regarded as cryptogenetic septico-pyæmia have this origin.

The importance of accessory and predisposing causes of inflammations due to bacteria is nowhere better illustrated than in the etiology of peritonitis, as has been set forth by Dr. Councilman on page 180. There are two principal classes of predisposing causes of peritonitis—namely, substances which damage the endothelial cells of the peritoneum, and solid, unabsorbable substances.

Of especial importance to the surgeon is a knowledge of the local and general predisposing causes of the infection of wounds. The general predisposing factors we shall consider later. From what has already been said, it is apparent that while the surgeon should use every effort to keep bacteria out of a wound, he should refrain so far as possible from doing anything which interferes with the power of the fluids and cells to overcome invading micro-organisms.

Among the local conditions[2] which have been found favorable to the growth in wounds of bacteria which otherwise might be disposed of by the tissues and animal fluids without harm may be mentioned strangulation of masses of tissue by ligatures; the presence of foreign bodies, such as drainage-tubes and coarse ligatures; interference with the circulation and absorption and the vitality of tissues resulting from undue pressure or tension; dead spaces; accumulation of the fluid and solid discharges from a wound, especially when associated with tension; necrosis and degeneration of tissues caused by the contact of strong chemical irritants. If it were within the power of the surgeon to keep bacteria entirely out of wounds or to destroy them without damage to the tissues after they enter, the conditions just mentioned could not by themselves alone cause infection, but this power he does not at present possess. The so-called aseptic wound of the surgeon is not usually aseptic in the bacteriological sense; that is, free from bacteria.

The following objections to the insertion of drainage-tubes into wounds have been elsewhere formulated by the writer:[3] *First*. They

[1] For the literature and the most important experiments and observations thus far made upon the subject of bacteria in hernial sacs consult Tavel and Lanz, "Ueber die Aetiologie der Peritonitis," *Mittheilungen aus Kliniken und med. Instit. d. Schweiz*, Basle and Leipzig, 1893; Arndt, "Ueb. d. Durchlässigkeit d. Darmwand eingeklemmter Brüche für Mikroorganismen," *ibid.*, 1893; and Tietze, *Arch. f. klin. Chirurgie*, Bd. 49.

[2] The writer wishes to acknowledge his indebtedness to his colleague, Dr. William S. Halsted of the Johns Hopkins Hospital, for information and numerous suggestions as to the influence of many local and general causes predisposing to the infection of wounds.

[3] Welch, "Some Considerations concerning Antiseptic Surgery," *The Maryland Medical Journal*, Nov. 14, 1891.

tend to remove bacteria which may get into a wound from the direct bactericidal influence of the cells and animal juices. *Second.* Bacteria may travel by continuous growth or in other ways down the sides of a drainage-tube, and so penetrate into a wound which they otherwise would not enter. We have repeatedly been able to demonstrate this mode of entrance into a wound of the white staphylococcus found so commonly in the epidermis. The danger of leaving any part of a drainage-tube exposed to the air is too evident to require mention. *Third.* The changing of dressings necessitated by the presence of drainage-tubes increases in proportion to its frequency the chances of accidental infection. *Fourth.* The drainage-tube keeps asunder tissues which might otherwise immediately unite. *Fifth.* Its presence as a foreign body is an irritant and increases exudation. *Sixth.* The withdrawal of tubes left any considerable time in wounds breaks up forming granulations, and thus both prolongs the process of repair and opens the way for infection. Granulation tissue is an obstacle to the invasion of pathogenic bacteria from the surface, as has been proven by experiment. *Seventh.* After removal of the tube there is left a tract prone to suppurate and often slow in healing.

The advantage from the employment of drainage-tubes or other drainage material is, of course, the removal of secretions, and this indication becomes an urgent one if the cavity with which the tube communicates is infected and suppurates. In a given case the surgeon must weigh the advantages and the disadvantages and act according to his judgment. The practice of most surgeons at the present time of restricting within much narrower limits than formerly the use of drainage-tubes, and of discarding them for all wounds which offer a fair prospect of primary union, is a distinct advance in the technique of antiseptic surgery.

The presence of blood in a wound is not itself to be desired, and modern surgeons justly lay stress upon prompt and careful hæmostasis in surgical operations. Blood in a wound is not, however, so dangerous a thing as some have supposed it to be, and where for the obliteration of cavities in a wound the choice lies between a blood-clot and the introduction of foreign substances, or the exercise of undue tension by sutures, or the application of a very large number of sutures, or forcible pressure, it is, as a rule, better to take the chances that the spaces will fill with blood (Halsted). Blood possesses bactericidal properties, and experiments made by the writer and Howard[1] showed that virulent pyogenic staphylococci injected into blood-clots which had been allowed to fill wound-cavities did not multiply and occasioned no suppuration. John Hunter was fond of dwelling upon what he called the vitality of blood, and John Chiene has directed attention anew to similar views. Schede brought prominently to the notice of surgeons the value of the blood-clot in the healing of a certain class of wounds, and Halsted[2] further extended the field of its application. The unintended presence of blood in a wound by occasioning undue tension and in other ways may be a dangerous thing, and is something very different from the purposeful application of

[1] Welch, "Conditions underlying the Infection of Wounds," *Transactions of the Second Congress of American Physicians and Surgeons*, vol. ii., 1891.

[2] Halsted, "The Treatment of Wounds with especial reference to the Value of the Blood-clot in the Management of Dead Spaces," *The Johns Hopkins Hospital Reports*, vol. ii. No. 5.

the method of healing by so-called organization of blood-coagula. It is of the first importance to prevent so far as possible all tension in a wound.

Undue stress is sometimes laid upon artificial devices to close the so-called dead spaces of a wound. These spaces when not drained, nor stuffed with foreign substances, nor obliterated by sutures or pressure, nor permitted to fill with blood, do not, unless very large, remain empty spaces. They quickly fill with exudations of fluids and cells, and these fluids and cells possess antibacterial properties as well as blood. For cavities with unyielding walls, such as those in bone, the blood-clot method of treatment has been found especially useful.

Surgeons are not agreed as to the value of the application of antiseptic fluids and substances to fresh wounds. There has been in recent years, under the name of aseptic surgery, a general tendency to consider them useless or harmful, but some surgeons still advocate the antiseptic irrigation of fresh wounds. The question is one which can be decided only by clinical experience. The experimental data bearing upon the question are the only ones appropriate to consider here.

The principal objections urged against the employment of the application of such disinfectants as corrosive sublimate and carbolic acid to fresh wounds are—*first*, that they accomplish little or nothing in the way of destroying bacteria which may have entered the wound; and, *second*, that they cause necrosis or other impairment of the tissues, and thereby weaken or abolish the antibacterial properties of the tissues, and thus predispose to infection.

The conditions for the destruction of bacteria by chemical disinfectants in the fluids and tissues of the animal body, even when the bacteria are only upon an exposed surface, are most unfavorable as compared with those in experiments with the same agents in test-tubes. The experiments of Schimmelbusch, already cited, do not, as he seems to suppose, demonstrate the uselessness of antiseptic applications to wounds in general. He found that the fatal infection of mice with the bacillus anthracis and that of rabbits with the bacilli of rabbit septicæmia, introduced in large number into fresh wounds, could not be prevented by the irrigation of the wound with corrosive sublimate (1 : 1000) or carbolic acid (5 per cent.) or other antiseptics. But some of the bacteria thus introduced, as has already been explained, are immediately or very soon absorbed from fresh wounds, and if one bacillus or a very few bacilli of the kind used by Schimmelbusch were thus absorbed, the death of the animal was sure to follow; whereas a similar absorption of a few ordinary pyogenic cocci is usually without significance. It is evident that these experiments are not conclusive as to the influence of antiseptics upon bacteria which remain in the wound, and are not applicable to the ordinary conditions of wound-infection during a surgical operation.

Henle[1] in his experiments conformed more closely to conditions of wound-infection in man. He found that in wounds of the rabbit's ear inoculated with streptococcus pus the streptococci remained in the wound for six hours, after which the cocci began to occupy the neighboring lymph-spaces. He found that regularly up to the end of the second hour a complete disinfection of the wound with sublimate (1 : 1000) or

[1] Henle, *Centralblatt für Chirurgie*, 1894, No. 30, *Beilage*.

carbolic acid (4 per cent.) could be attained, and that even after six hours the disinfection sometimes prevented the development of the disease, and, if not completely successful, rendered the subsequent infection milder than in the inoculated control ear which was not disinfected.

Löffler has shown by his careful tests of the action of various antiseptic substances upon diphtheritic throats that it is possible to destroy the superficial bacteria by antiseptics without serious injury to the tissues. It is possible that disinfectants, without actually killing bacteria, may restrain their power of development or weaken their virulence.

Messner[1] experimented by inoculating fresh wounds of rabbits with pus or with cultures containing pyogenic cocci, which caused progressive phlegmonous inflammation with fatal termination. He found that, with one exception, all of the ten wounds inoculated with the cocci, and then irrigated with sterile salt-solution and treated aseptically, suppurated, with the development of progressive phlegmons which killed the animal within two weeks. On the other hand, all of the ten wounds, with one exception, similarly inoculated and treated antiseptically with lysol or 3 per cent. carbolic-acid solution, healed and the animals survived. Two of the wounds treated antiseptically healed without suppuration; the remaining eight suppurated, showing that the cocci had not actually been destroyed, but the process remained localized. Pus from the wounds treated aseptically preserved its virulence, whereas pus from the wounds treated antiseptically was devoid of virulence when inoculated into animals.

Hermann and others have shown that if carbolic acid, corrosive sublimate, and various other chemical irritants be injected subcutaneously into the tissues and soon afterward pyogenic micro-organisms be injected into the same locality, the formation of an abscess is much more likely to follow than when the bacteria are injected into the healthy tissues. But, as Messner has shown, a similar favoring influence upon the development of suppuration under these circumstances is exerted by the injection of common salt-solution into the subcutaneous tissues. These experiments are not applicable to the conditions existing in an open wound, but they confirm clinical observations as to the great danger of introducing into the subcutaneous tissues of man, with a hypodermic syringe, fluids containing pyogenic bacteria.

Unquestionably, the presence of necroses, such as may be produced by strong chemical disinfectants, predisposes to pyogenic infection. In some situations, as in a closed cavity like the peritoneal, the presence of even superficial necroses, which may affect only the endothelial cells, is an important predisposing cause of infection, but only experience can decide whether such slight superficial necrosis or other injury which the ordinary antiseptics may produce in an external wound is in itself an important predisposing factor in the pyogenic infection of wounds, or even if a predisposing factor is not more than counterbalanced by beneficial influences exerted by the application of antiseptics. Messner has reported experiments on rabbits which seem to show that the irrigation of fresh wounds with 3 per cent. carbolic-acid solution does not lessen the vital resistance of the tissues in a wound to subsequent inoculation with pyogenic cocci.

[1] Messner, *Ibid.*

Experiments upon animals, therefore, favor rather than oppose the antiseptic treatment of wounds, as distinguished from so-called asepsis.

We turn now to the consideration of local predisposition existing at some point within the body, the so-called locus minoris resistentiæ. After the infectious agents have passed through the portal of entry and entered the general circulation they may find local conditions favoring their lodgement and development. Without such local predisposition they are often incapable of doing any harm.

Injury, inflammation, and other pre-existing disease of an internal part are important and common conditions favoring the lodgement and growth of micro-organisms. The classical experiment of Chauveau many years ago demonstrated the predisposition of injured internal parts to infection. He twisted off without rupture of the skin one of the testicles of a young ram from its vascular connections (bistournage), and observed that when he had injected shortly before the operation putrid fluid containing micro-organisms directly into the circulation the injured testicle became the seat of septic gangrene, while without such injection the testicle became necrotic and was absorbed without becoming infected.

The experiments of Rosenbach, Orth and Wyssokowitch, Prudden, and others have shown that bacteria do not readily become attached to the smooth surface of the heart-valves, but that pyogenic cocci readily adhere and set up septic endocarditis when the valves have been previously torn by a sterile probe passed down the carotid artery. The predisposition of injured joints and bones to the settlement of pyogenic cocci and of tubercle bacilli is established both by clinical and experimental observations. Pyogenic cocci often invade foci of disease caused primarily by other organisms, as is exemplified in tuberculous and gonorrhœal arthritis, actinomycosis, echinococcus cysts, amœbic abscesses of the liver, etc. In some situations, particularly in the kidney and urinary tract, the colon bacillus often settles in pre-existing foci of disease. The anæmic and dry condition of the lung induced by pulmonary stenosis favors the development of pulmonary tuberculosis. The hyperæmic and moist condition associated with mitral regurgitation is comparatively unfavorable to such development, although by no means excluding this disease. Pyogenic cocci not infrequently settle in the joint-lesions of locomotor ataxia and cause suppuration.

The existence of a diseased or injured part within the body by no means involves, of necessity, the localization therein of infectious processes which may be caused by pathogenic micro-organisms in the circulation. The damaged part may be spared and an apparently healthy part attacked. The endeavor to obtain experimentally in animals the localization of suppuration in a fractured bone or other injured or diseased part by pyogenic cocci injected into the circulation often fails, and in the hands of Rinne failed so regularly that he opposes, although without sufficient reason, the whole doctrine of locus minoris resistentiæ. By a different line of experimentation Gottstein came to the same conclusion as Rinne.

We are undoubtedly able in some cases to explain the localization of an infection by such apparent local predisposing causes as those which have been mentioned, but in many, indeed in the majority of, instances of localized infections of internal parts we are unable to give any satis-

factory explanation of the localization. We know that many pathogenic micro-organisms have a decided preference for certain organs and tissues. The injection of the staphylococcus aureus into the circulation of rabbits does not lead to the formation of abscesses in all parts of the body, although the cocci must be carried by the blood-current everywhere. The abscesses are found most frequently in the kidneys and myocardium, sometimes in the muscles elsewhere, and in young rabbits often in the bone-marrow and joints. To say that the tissues in one part of the body offer better conditions for the growth of the micro-organisms than in other parts is only another way of saying that the organisms produce disease in one part and not in another. Such phrases offer no real explanation unless the nature of these better conditions can be defined.

Sometimes we can explain the localization by the manner of reception of the virus, the vascular relation of the part to infected areas, the size and number of the capillaries, the velocity of the circulation, and the readiness with which foreign particles are filtered out. We know that fine particles are deposited from the lymphatic current in the lymph-glands, and from the blood-circulation chiefly in the spleen, marrow of the bones, liver, and lymph-glands. More often we are unable to give any adequate explanation of the localization of an infectious process in internal parts of the body.

General Predisposition.—Under this heading we shall consider predisposing causes which act more or less generally upon the whole body. The effect of such causes may be to increase the susceptibility of the whole body or only of particular parts of the body to infection. The factors here concerned are for the most part less tangible than the local causes of predisposition.

Organs and parts of the body may inherit special vulnerability to certain infections. Susceptibility to certain infectious diseases may be manifest in races and families. The negro race is less susceptible to yellow fever than the white. Algerian sheep are in large measure insusceptible to anthrax, which is very fatal to other sheep. Black rats are more resistant than gray, and gray rats more resistant than white, to anthrax (Müller).

Age influences predisposition, as regards some infectious diseases favorably, as regards others unfavorably. Wounds in children, as a rule, heal more quickly, and with less danger of suppuration should pyogenic bacteria enter, than in old people. Certain infectious diseases are most common in infancy, others in adolescence or in maturity or in old age. Osteomyelitis is much more common in children than in adults. This has been attributed to the predisposing influence of injuries to which children are more liable. Doubtless injuries enter into the causation as a predisposing factor, but it has been shown experimentally that there is a special susceptibility of the bone-marrow of young growing animals to infection by pyogenic cocci injected into the circulation (Rodet, Colzi, Courmont and Jaboulay, Lannelongue and Achard, Lexer). In laboratory experiments young animals, as a rule, are found to be more susceptible to most pathogenic bacteria than old ones. There is a special insusceptibility of sucklings during the first months of life to certain infectious diseases, such as mumps, measles, scarlet fever. As will be explained

later, the embryo possesses remarkable insusceptibility to some infections.

There is no evidence that there is any difference in predisposition to infection between males and females, except as regards infections directly related to sexual functions.

General anæmia, induced by loss of blood, has been shown experimentally to increase susceptibility to infection with various micro-organisms, including the pyogenic cocci, Friedländer's bacillus, and the anthrax bacillus (Rodet, Gärtner, Chauveau, and others). Operative and other wounds are more likely to suppurate when there has been much hemorrhage than when the loss of blood is slight. In general, impaired vitality and nutrition of the body may predispose to certain infections, including wound-infection. More or less plausible predisposing causes operating in this way are bad and insufficient food, overwork, depressing emotions, exposure to heat or cold, overcrowding, bad air, and, in general, insanitary surroundings and all conditions of misery.

A large number of experiments have been made upon animals to determine the influence of various factors in increasing susceptibility to infection. The results of these experiments are interesting and suggestive in many ways. Some of them evidently correspond to conditions observed in man, but it is to be remembered that without additional evidence we have no right to apply the results directly to human beings, or to any other bacteria or other animals than those experimented with. The more important results of these animal experiments are the following:

Prolonged narcosis may impair resistance to some pathogenic micro-organisms. Klein and Coxwell made frogs and rats highly susceptible to anthrax by narcosis with ether and chloroform, and similar results have been obtained with curare, alcohol, chloral, morphine, and upon other animals and with other diseases. In speaking of the effect of anæsthetics in predisposing to wound-infection Roswell Park [1] says: "There is good reason to think that chloroform and ether administered for some time may produce such changes in the blood and tissues that vital processes of repair, cell-resistance, and chemotaxis may be so far interfered with as to facilitate subsequent infection."

Feser, Hankin, and Müller found that rats fed on bread are more susceptible to anthrax than those fed on meat. Müller observed the same degree of insusceptibility when the extractive substances from meat were fed.

Canalis and Morpurgo, and Sacchi rendered pigeons highly susceptible to anthrax by hunger, and Bouchard noted the lowering or disappearance of artificial immunity in rabbits from anthrax by starvation. Prolonged abstinence from water was observed by Pernice and Alessi to render relatively insusceptible animals more susceptible to anthrax. Charrin and Roger found in fatigue induced by working a treadwheel a factor which increased the susceptibility of rats to anthrax and symptomatic anthrax.

Various chemical substances introduced into the body may increase susceptibility to certain infections. Gottstein and Mya and Sanarelli have shown that poisons, such as chlorates, pyrogallic acid, pyridin,

[1] Park, *loc. cit.*

which destroy red blood-corpuscles, may render insusceptible animals highly susceptible to certain pathogenic micro-organisms, although hæmatolysis thus produced in the case of some animals and certain micro-organisms did not weaken natural immunity. Bonome found that hæmatolysis and hæmoglobinuria caused by injection of water into the circulation of rabbits lessened the bactericidal power of the blood as regards the staphylococcus aureus. By feeding white mice with phloridzin, which produces glycosuria, Leo rendered these animals highly susceptible to glanders, from which normally they are immune.

The most important class of experiments showing the predisposing influence of certain chemical substances upon infection are those in which various ferments and bacterial products have been used. In considering bacterial association (page 291) attention has already been called to the fact that the chemical products of some bacteria favor the development of infection with other bacteria. The susceptibility of an animal to infection with a specific micro-organism can often be increased by the preliminary or simultaneous injection of the products of the organism. It is not only the products of pathogenic bacteria which may thus increase susceptibility, but also those of certain saprophytic varieties, particularly of the ordinary putrefactive bacillus proteus. Nor is it necessary that the bacterial products in order to weaken resistance to infection should cause distinct toxic symptoms. We do not possess any satisfactory experimental evidence that the volatile and stinking products of putrefactive decomposition augment susceptibility to infection.

Park, Bouchard, and others lay much emphasis upon auto-intoxication from absorption of fermentative products in the stomach and intestine as a predisposing cause of infection, particularly with the pyogenic cocci. Neumann and Canon, in order to test the predisposing influence of absorption of fermentative products from the intestine, ligated aseptically the small intestine of rabbits near the ileo-cæcal valve and injected subcutaneously a streptococcus culture. The animals with intestinal obstruction, with few exceptions, died with streptococcus septicæmia, whereas the streptococci injected into normal rabbits produced only local inflammation at the point of injection. The ligation of the intestine close to the stomach was not followed by generalization of the streptococcus infection. So deadly an operation as ligation of the intestine introduces so many other factors than the possible absorption of poisonous intestinal products that these experiments cannot be considered to prove what they were intended to demonstrate. Extirpation of the kidneys, with subcutaneous injection of streptococci, also leads to general streptococcus infection.

That many acute and chronic diseases lower the resistance of the body to pathogenic micro-organisms has repeatedly been mentioned in the course of this article, and is universally admitted. The influence of certain infectious diseases in favoring the development of secondary and mixed infections has been sufficiently referred to.

Diabetes mellitus is well known to increase in a marked degree the susceptibility to infection, particularly with pyogenic cocci and the tubercle bacillus. Among other diseases characterized by lessened resistance to infection may be especially mentioned acute and chronic Bright's disease, arterio-sclerosis, cardiac disease, alcoholism, syphilis, rickets,

scurvy, leucocythæmia, Hodgkin's disease. All of these diseases are prone to lessen resistance to pyogenic cocci, and especially to the streptococcus pyogenes. A localized streptococcus infection is much more likely to become generalized when it develops in persons affected with any of these diseases than when it appears in a previously healthy person. Here also attention may be called to the terminal streptococcus septicæmias occurring in Bright's disease, heart disease, and various chronic diseases. They may not be distinguished by characteristic symptoms during life, and are to be ranked among such events as terminal pneumonia and dysentery. The portal of entry is most frequently the lungs, skin, and intestine.

Of 218 autopsies of chronic Bright's disease, general arterio-sclerosis, and chronic heart disease at the Johns Hopkins Hospital, in 154 there were definite infections. Of 32 cases of local streptococcus infection, excluding perforative peritonitis, tabulated from the autopsy records of the hospital by the writer, chronic nephritis, general arterio-sclerosis, or chronic heart disease was present in 18. In 11 out of 14 cases of general streptococcus infection one or more of these diseases was present. We have observed several cases of general streptococcus infection in leucocythæmia and Hodgkin's disease.

In a large number of cases we are able to find no explanation of the existence of individual predisposition.

In conceding to predisposition its full importance as a factor in the etiology of surgical infections, we are not to forget that pyogenic cocci occur of such virulence that they can readily overcome the natural resistance of the most insusceptible human being.

Fœtal Infection.

The embryo may be infected by transmission of the specific micro-organism with the ovum or semen. The only example of this germinal infection in which the conditions are thoroughly understood is pebrine of silkworms caused by sporozoa, which have been studied in all stages of transit through the ovum and spermatozoa to the infected offspring.

The only infectious disease of human beings which has been proven to be capable of conveyance to the offspring through the ovum or spermatozoa is syphilis. Congenital syphilis is usually due to germinal infection, and it may come from either a syphilitic father or a syphilitic mother.

Intra-uterine or placental infection of the fœtus may occur in many infectious diseases. Although the intact placenta is a perfect physiological filter, which does not permit the passage of inanimate particles from the blood of the mother to that of the fœtus, nevertheless pathogenic micro-organisms are capable of breaking through this barrier. The conditions which permit the passage of micro-organisms from mother to fœtus can sometimes be demonstrated in the form of definite lesions of the placenta, either pre-existing or caused by the specific micro-organisms or their products. Circulatory disturbances, hemorrhages, defects in the epithelium covering the chorion villi, areas of necrosis, and tubercles in the placenta have been observed with more or less frequency in cases of fœtal infection, but often no placental lesion could be detected.

In the later stages of pregnancy and during parturition the anatomical and physiological conditions would seem to be more favorable for the escape of micro-organisms from the mother's blood to the fœtus than in the early stages.

Some micro-organisms are much better adapted than others to pass through the placenta from mother to fœtus. In animals the bacilli of chicken cholera and of symptomatic anthrax and the pyogenic cocci frequently make this passage. Although there has been much controversy as to anthrax, it is now settled that anthrax bacilli often pass from mother to fœtus, but generally in such small numbers and without subsequent multiplication in the fœtus as to require special methods and careful search for their detection.

In human beings infection of the fœtus in utero has been observed in small-pox, measles, scarlet fever, relapsing fever, syphilis, tuberculosis, croupous pneumonia, typhoid fever, anthrax, and affections caused by pyogenic cocci. In general, such infection is exceptional, but in some diseases it is comparatively common. Surgical importance attaches to the fact that both experiments on animals and clinical observations show that the pyogenic cocci are frequently transmitted to the fœtus from an infected mother.

Developed tuberculosis in the new-born infant is extremely rare, although it has been observed, but this rarity does not prove that tubercle bacilli may not often be transmitted from mother to fœtus. It takes time and susceptibility for tubercle bacilli to produce recognizable lesions. Tubercle bacilli without developed tuberculosis have been repeatedly found in the fœtus of tuberculous mothers. Birch-Hirschfeld detected in a seven-months' fœtus, removed by Cæsarean section from a mother with acute miliary tuberculosis, tubercle bacilli both by microscopical examination and by inoculation of guinea-pigs. There were no tuberculous lesions in the fœtus. The failure to find tubercle bacilli in a large number of similar cases can hardly be regarded as proof of their absence, when one considers the difficulty of demonstrating tubercle bacilli in small number irregularly distributed through a large mass without any lesion to indicate where they are most likely to be found. Gärtner finds that the transmission of tubercle bacilli from mother to fœtus is common in the experimental tuberculosis of mice, rabbits, and canary birds.

There is reason to believe that the embryo offers great resistance to the growth of tubercle bacilli. Maffucci has found that tubercle bacilli inoculated into hens' eggs before incubation remained quiescent during the period of embryonic development, but caused the death of most of the chicks from tuberculosis in three weeks to four and a half months after birth. We have evidence that in human beings living and virulent tubercle bacilli may remain latent in the body a long time. As already mentioned, the chances of penetration of bacilli into the fœtus appear to be more favorable during the later period of pregnancy than earlier. The frequency of tuberculosis increases very rapidly with each succeeding week after birth, until during the second half of the first year and during the second year of life fatal tuberculosis is very common, and then becomes less frequent until after puberty. Infantile tuberculosis is far more commonly situated in internal organs, such as the lymphatic glands,

meninges, bones, and joints, without tuberculous lesion on any exposed surface of the body, than is tuberculosis of adults.

These are the arguments which are urged by Baumgarten and others with great force in favor of frequent bacillar heritage. The majority of authorities, however, are reluctant to abandon the older views, and the final settlement of this important question involves great difficulties not likely to be soon overcome.

The portal of entry to the fœtus is the umbilical vein, and therefore micro-organisms would be carried first to the liver and the right side of the heart. Corresponding to this, we find that lesions of the liver and of the right side of the heart are particularly common in congenital infections. Pyogenic cocci, as already mentioned, break through the placental barrier with comparative ease, and these are the bacteria most often associated with endocarditis, which is more common on the right side of the heart in the fœtus and new-born than in the adult.

Although the fœtus may react to pathogenic micro-organisms in the same way as the mother, or even more severely, it possesses a remarkable insusceptibility to some infections, as has been proven experimentally and clinically. There are several instances in which the specific bacteria of croupous pneumonia and of typhoid fever have been found in the stillborn embryos of mothers affected with these diseases, but there is no satisfactory recorded instance of an infant born with the lesions of typhoid fever or those of lobar pneumonia caused by the pneumococcus. Some bacteria which cause localized infections in the mother may produce in the fœtus general septicæmia without localizations.

General Considerations concerning Pyogenic Bacteria.

The pyogenic bacteria play such a predominant rôle in surgical infections, and their pathogenic characters present so many peculiarities, that it is appropriate to consider here the general relations of pyogenic bacteria to surgical infections, although the consideration of the special diseases caused by these bacteria does not fall within the scope of this article.

There are no specific bacteria of suppuration. On the one hand the number of bacteria which under special conditions are capable of causing suppurative inflammation is large, and is not limited to any particular group, and on the other hand the bacteria which are most frequently the cause of suppuration are capable of causing other forms of inflammation and of producing infection without inflammation.

Certain staphylococci and streptococci, however, are found in purulent inflammations in human beings so much more frequently than other micro-organisms that they are the pyogenic bacteria *par excellence*, and are the ones generally understood when the expression "micro-organisms of pus" or "pyogenic bacteria" is used without any qualification. These staphylococci and streptococci are endowed with pus-producing properties in larger measure than are other bacteria, and of all their pathogenic effects the production of suppurative inflammation is the most prominent.

The most common pyogenic cocci are the staphylococcus pyogenes aureus, the streptococcus pyogenes, and the staphylococcus pyogenes

albus, including the staphylococcus epidermidis albus. In the second rank, as regards both frequency and virulence, are the staphylococcus pyogenes citreus, the staphylococcus cereus albus, and the staphylococcus cereus flavus. More common and far more important than the cocci of the latter group are the micrococcus lanceolatus and the micrococcus gonorrhœæ. Although these are not always ranked among the pyogenic cocci in the restricted sense, they are genuine pus-producers. The micrococcus tetragenus septicus is rarely the sole cause of suppuration. The status of the micrococcus pyogenes tenuis is uncertain. It is perhaps identical with the micrococcus lanceolatus.

There is a long list of bacilli which have been shown with greater or less certainty to be capable of producing suppurative inflammations in man. The principal ones are bacillus pyogenes fœtidus, bacillus coli communis, bacillus typhi abdominalis, bacillus tuberculosis, bacillus pyocyaneus, bacillus pneumoniæ of Friedländer, bacillus proteus. Actinomyces belongs to the class of schizomycetes and is a pus-producer.

Several anaërobic bacilli have been found both in pure culture and associated with other bacteria in closed abscesses. Of these may be especially mentioned bacillus phlegmones emphysematosæ of E. Fraenkel, which is probably identical with bacillus aërogenes capsulatus previously described by Welch and Nuttall, and which occurs in some phlegmons containing gas.

The list of demonstrated pus-producing bacteria is by no means exhausted by those enumerated. In the experience of the writer bacilli are more common causes of spontaneous abscesses in laboratory animals than cocci. A very large number of bacteria are capable of producing experimental abscesses in animals.

It is fair to say that not all of the bacteria mentioned above are recognized as pyogenic for man by all authorities, and particularly that some do not so regard the typhoid bacillus and the tubercle bacillus; but in the opinion of the writer their pyogenic capacity has been demonstrated.

We have very little definite information as to the underlying conditions which control the pyogenic manifestations of such bacteria as the typhoid bacillus, the tubercle bacillus, and others which do not ordinarily cause purulent inflammations. These conditions seem to pertain partly to the degree of virulence of the micro-organism and partly to the local susceptibility of the tissues invaded and the general susceptibility of the individual. We find in experiments upon animals that bacteria of weakened virulence in susceptible animals, or those of usual virulence in insusceptible animals, are prone to produce localized abscesses. In an animal which has been rendered artificially immune from septicæmia caused by certain pathogenic bacteria immunity is not usually produced from the development of local abscesses by the specific organism, in case this is capable of forming abscesses.

Statistical statements as to the relative frequency with which the different pyogenic cocci occur in general in suppurative and septic affections vary according to the class of cases which preponderate. The staphylococcus aureus is by far the most common micro-organism in furuncles and osteomyelitis, and is common in circumscribed subcutaneous abscesses. The streptococcus pyogenes is by far the most common organism in

spreading phlegmonous cellulitis, inflammations of serous membranes, puerperal infections, and septicæmia. It is the cause of erysipelas in practically all cases of this disease. It is a frequent cause of all kinds of inflammations of the throat and of broncho-pneumonia. The staphylococcus albus is often associated with the other pyogenic cocci, especially in inflammations involving the skin. It occurs most frequently in the same general class of cases as the staphylococcus aureus. Although capable of causing grave infections, the characters of the inflammations in which the white staphylococcus is found alone are usually mild. Two or more species of pyogenic cocci are often combined.

The relative frequency of occurrence of the pyogenic cocci seems to vary somewhat according to the locality. Levy finds in Strassburg the staphylococcus albus more frequently than the staphylococcus aureus in all suppurative affections except furuncles, and he was unable to confirm the usual statement that the albus is less virulent than the aureus.

The following table gives the results of the bacteriological examination of 135 ambulatory and operative surgical cases by Dowd[1] in the Vanderbilt Clinic and Cancer Hospital in New York. It affords a good idea of the relative frequency of the different pyogenic cocci in the class of cases which most frequently come to the attention of the surgeon:

	Cellulitis, 51 cases.	Infected fresh wounds, 17 cases.	Old granulating wounds, 18 cases.	Healing wounds, stitches, 5 cases.	Furuncles, 7 cases.	Abscesses, 37 cases.
Streptococcus pyogenes alone	9	3	. .	. .	. .	8
Streptococcus pyogenes predominant	23	3	. .	. .	. .	8
Streptococcus pyogenes relatively few	3	1	6	. .	. .	1
Staphylococcus pyogenes aureus alone	11	1	1	1	7	6
Staphylococcus pyogenes aureus predominant	8	2	. .	. .	. .	1
Staphylococcus pyogenes aureus relatively few	13	3	. .	. .	. .	2
Staphylococcus pyogenes or epidermidis albus alone	1	4	2	4	. .	2
Staphylococcus pyogenes or epidermidis albus predominant	. .	1				
Staphylococcus pyogenes or epidermidis albus relatively few	10	5	3	. .	. .	6
Staphylococcus cereus albus	3	1	2	. .	. .	1
Staphylococcus citreus	1	. .	2	. .	. .	1
Bacillus pyocyaneus	. .	. .	1	. .	. .	3
Bacillus coli communis	. .	. .	. .	. .	. .	3
Very few growths on agar	. .	. .	3	. .	. .	3
No growths on agar	. .	. .	. .	. .	. .	11
Few undetermined colonies	12	2	5	. .	. .	5

The cases from which no growth occurred were tuberculous abscesses and buboes. 8 of the 51 cases of cellulitis showed a persistent tendency to spreading inflammation with undermining of the tissues. In all of these 8 cases streptococci were found. In 2 cases of pyæmia staphylococcus aureus and streptococci were present in the original wound, but only streptococci in the metastases.

It is interesting to contrast with these results of the examination

[1] Charles N. Dowd, "Some Considerations on Different Types of Exudative Inflammation," *Medical Record*, New York, Sept. 8, 1894.

of ambulatory and operative surgical cases the results of the bacteriological examination of post-mortem cases. In about 500 autopsies at the Johns Hopkins Hospital there were found in 185 cases the following bacteria:

	Number of cases.
Bacillus coli communis	105
Streptococcus pyogenes	62
Staphylococcus pyogenes aureus	43
Micrococcus lanceolatus	29
Staphylococcus pyogenes albus	14
Bacillus typhosus, as the cause of special complications	7
Bacillus pyocyaneus	8
Proteus	4
Micrococcus tetragenus	2
Staphylococcus pyogenes citreus	1
Pneumobacillus of Friedländer	1
Bacillus pyogenes fœtidus	3
Bacillus aërogenes capsulatus	3
Undetermined bacteria	35

The streptococcus cases do not include those in which streptococci were found only in phthisical cavities or adjacent lung. The cases with micrococcus lanceolatus are those in which this organism was found without pneumonia or as the cause of some extra-thoracic complication of pneumonia. No cases are included in which the bacteria were found simply on exposed surfaces of the body. Among the undetermined bacteria are several interesting pathogenic forms which could not be positively identified with species already described. Mention has already been made of the frequent invasion of the colon bacillus without any pathogenic manifestations.

The preceding table is inserted not with the intention of analyzing in this article the cases[1] composing it, but to show the great differences between the results of the bacteriological study of living surgical cases and those of the autopsy material of a general hospital, and especially to emphasize the preponderance of streptococcus cases over staphylococcus and all other pyogenic cases in such material.

All of the affections caused by one species of the pyogenic cocci may be caused by any of the others. For example, the staphylococcus aureus may produce spreading phlegmons, inflammations of serous membranes, puerperal infections, general septicæmia as well as the streptococcus pyogenes, and the streptococcus pyogenes may cause circumscribed abscesses and osteomyelitis as well as the yellow or white staphylococcus. Jordan claims that the staphylococcus aureus may cause erysipelas, but Petruschky does not regard his observations on this point as conclusive.

Furthermore, these pyogenic staphylococci and streptococci may cause all kinds of inflammation besides the suppurative. They may, and often do, cause serous, sero-fibrinous, and fibrinous inflammations of serous membranes. The streptococcus pyogenes may cause catarrhal and fibrinous inflammations of mucous membranes. Pyogenic cocci may be the cause of simple inflammatory œdema or serous infiltration of the tissues. They are sometimes found in cutaneous vesicles and blebs containing clear serum. They may be the sole organisms present when

[1] The analysis of these cases was the subject of the Middleton Goldsmith lecture by the writer in April, 1894 (*Trans. N. Y. Pathological Society* for 1894).

the inflammatory exudate is hemorrhagic. They may produce extensive necrosis of the tissues with scarcely any inflammatory exudate. We find the same staphylococci and streptococci in those rarer forms of osteomyelitis which do not suppurate as in the ordinary suppurative form. They are the usual cause of periostitis and ostitis albuminosa, in which the exudate is serous. A serous or sero-fibrinous inflammation caused by pyogenic cocci may be transformed into a purulent one without the appearance of any new species of micro-organism.

We cannot at present give any satisfactory explanation of these diverse effects produced by one and the same bacterial species. We seek to explain these differences usually by referring to such factors as the degree of virulence of the organism, the manner of its invasion, the site of infection, and the condition of the patient. Variations in virulence and the general condition of the patient cannot be the sole explanation, for these pyogenic cocci may in the same individual cause a suppurative inflammation in one part of the body and a serous or a sero-fibrinous inflammation in another part, without any bacteriological difference. We have observed this in some instances of multiple serositis, and Schrank has reported a case in which periostitis albuminosa was associated with suppurative osteomyelitis in the same tibia. The same micro-organisms, staphylococci and streptococci, were present in the exudate in both situations. They had produced pus in the bone-marrow and a simple serous exudate between the periosteum and bone. The deciding factor must have been in the tissues, and not in the micro-organisms or the general predisposition of the individual, and this same factor, the specific character of the tissues, little as we may comprehend its nature, is doubtless the explanation of their varying reactions to the same infectious agents in many other cases—a point which has been justly emphasized by Kurt Müller.

It might be inferred from what has been said as to the interchangeable effects produced by the different pyogenic cocci that no diagnostic or prognostic importance is to be attached to the determination of the particular species of pyogenic coccus present. If the streptococcus can do everything which the staphylococci can do, if each species can produce mild as well as grave infections, it is argued by some that it is of no practical importance to determine what particular micro-organism is present in a given case.

It is more important for the surgeon to understand the general relations of bacteria to traumatic and other pyogenic infections than to become familiar with the special characters of the individual micro-organisms which cause these infections, and therefore the principal part of this article has been devoted to a consideration of these general relations. But apart from the interest which pertains to the study of all aspects of disease, even those without evident practical bearings, it would be a mistake to suppose that the bacteriological examination of infectious processes caused by pyogenic cocci is devoid of value for diagnosis, prognosis, or treatment.

There are certain general rules as to the characters of the infections most likely to be produced by the different species of pyogenic cocci, and as to the probability of finding a given species in a certain kind of infection. It would lead too far to attempt to consider here all the differ-

ent surgical infections with reference to these points. A few illustrative examples may be cited.

The white staphylococcus causes severe local and general infections so infrequently, at least in this country so far as we are informed, that the recognition of its exclusive presence in an inflamed external part of the body justifies the probable conclusion that the inflammation will pursue a mild course and be readily amenable to treatment.

The streptococcus pyogenes may possess all degrees of virulence. Although a streptococcus coming from a case of erysipelas or puerperal fever may not be distinguished botanically from a streptococcus coming from a healthy mucous membrane or caught from the air, it is a very different thing in its possibilities for infection. The streptococcus pyogenes, far more frequently than other bacteria, causes spreading phlegmonous inflammations and grave forms of septicæmia. The importance and the frequency of streptococcus septicæmias accompanying tuberculosis, diphtheria, typhoid fever, scarlet fever, the puerperal state, erysipelas, cellulitis, and traumatic infections are probably not even yet sufficiently appreciated by physicians and surgeons, notwithstanding the rapid extension of our knowledge of this subject in recent years. Septicæmias produced by other pyogenic cocci under these circumstances, although they may be of equal severity and similar character, are in a small minority.

In view of the fearful pathogenic possibilities with which streptococci may be endowed, a surgeon cannot regard the presence of these micro-organisms in a wound or inflamed part with as little concern as he may the white or even the yellow staphylococcus, although it may be that the particular streptococcus in question is of relatively slight virulence. If his patient have chronic Bright's disease or general arterio-sclerosis or chronic cardiac insufficiency, the anxiety of the surgeon will be increased. Inflammations of external parts produced by staphylococci are in general more amenable to treatment and require less vigorous interference than those caused by streptococci. Streptococcus cases are in general more dangerous to other surgical patients in their proximity than staphylococcus cases, and are therefore more likely to require isolation.

The gravest staphylococcus infection with which the surgeon has commonly to deal is acute osteomyelitis. In this particular field the staphylococcus aureus takes rank over the streptococcus, although there is no specific micro-organism of osteomyelitis any more than there is of suppuration in general. Osteomyelitis may be caused by the streptococcus pyogenes and other pyogenic bacteria, but, although these other bacteria not infrequently cause periostitis, they are very rarely the cause of uncomplicated suppurative osteomyelitis.

The especial conditions under which, in cases of infection caused by pyogenic cocci, the cocci appear in the blood in sufficient number to be demonstrable by our methods of examination are far from clear. We find them far more frequently in the blood at autopsies, even very fresh ones, than we are able to do during life. The pyogenic cocci, like most pathogenic bacteria, only exceptionally are able to multiply in the circulating blood of human beings. The greater frequency of their presence in demonstrable number at autopsy may be due in part to their multiplication after death, but this cannot be the sole explanation, as the cocci are found in autopsies made very early after death more frequently than

they are found during life. The explanation is probably that during the last hours of life they often find suitable conditions for their multiplication in the blood. A similar phenomenon can often be observed in inoculated animals. All bacteria, including those of the typical septicæmias of animals, such as the bacillus of rabbit septicæmia, of anthrax, the micrococcus lanceolatus, injected into the blood quickly disappear from the circulation. The pathogenic forms grow outside of the circulating blood, and often do not make their reappearance in any considerable number in the circulation until shortly before death and after the manifestation of grave constitutional symptoms. This is true of pneumococcus septicæmia, anthrax, and other typical septicæmias of animals.

In examining the blood of living patients for pyogenic cocci a few drops of blood do not generally suffice, as the cocci are rarely so numerous as to be detected thus. The blood is obtained by wet cups by Petruschky, who has developed a special technique for these examinations. To the demonstrations of the white staphylococcus in blood withdrawn by cutting or pricking the skin, which have been made by a number of investigators, the writer attaches no diagnostic significance, for reasons which have been stated. The detection of streptococci is significant. Petruschky and Canon found streptococci in the blood during life in a number of cases of pyæmia, septicæmia, and localized infection. They were more likely to be present in severe than in the milder cases, but they were occasionally found in cases which recovered, and even in very mild infections. Cocci are found in the blood in cases both with and without metastases.

Doubtless pyogenic cocci often enter the circulation in small number from a localized focus of inflammation caused by them. They are often disposed of without doing any harm by the bactericidal cells and fluids. Their fate, however, is not always one which is so advantageous to the patient. They may lodge and grow in internal parts, causing inflammations of serous membranes, ulcerative endocarditis, and other metastatic inflammations. They may survive, and even multiply, in the blood, with or without the production of metastases. These general infections, particularly those with the streptococcus pyogenes, are far more likely to occur with primary localized infections, such as erysipelas, infected wounds, abscesses, in persons with chronic Bright's disease, and other conditions which we have repeatedly specified as predisposing causes, than in previously healthy persons.

The usage has grown up among bacteriologists of limiting the name "septicæmia" to infections characterized by a large multiplication of bacteria in the blood during life. Septicæmias in this bacteriological sense occur in man, but they are not common. Far more common are cases of human septicæmia in which a moderate or small number of pyogenic cocci are found in the blood, but there is no definite relation between the number of bacteria in the blood and the character and gravity of the symptoms. We cannot explain these symptoms nor some of the lesions without assuming that they are referable to the action of toxic products of the bacteria, and that these toxic products may be absorbed from localized foci of inflammation.

There are no specific bacteria of either septicæmia or pyæmia. The same bacteria are found in both diseases.

Bacteria of Surgical Infections.

The leading characters, especially the pathogenic, of the bacteria concerned in surgical infections will here be briefly described. Certain rare and unnamed and insufficiently identified bacteria which have been described as occurring in surgical diseases will not be considered.

Staphylococcus Pyogenes Aureus (Plate II., Fig. 5).—Observed by Ogston (1881), first accurately described by Becker (1883), Rosenbach (1884), and Passet (1885). Appears in the form of spherical cells, averaging 0.8 μ in diameter, which by differential staining often show a diplococcus or biscuit shape. Occurs usually in clumps, also in pairs and short chains. May be found both within and outside of pus-cells in abscesses. Stains readily with aniline dyes, including Gram's stain. Forms an orange-yellow pigment, but only in the presence of free oxygen. Grows at ordinary temperatures, most rapidly at body temperature. Grows on all culture media both with and without free oxygen. Liquefies gelatin rapidly. Coagulates milk; clouds bouillon. May survive in dried pus for one hundred days; is killed in a much shorter time by desiccation when contained in thin media. In the moist condition is killed in ten minutes by a temperature of 58° C. (Sternberg). When dried a higher temperature—90–100° C.—is required to kill it in a short time. In bouillon cultures all of the cocci may be killed in five minutes by sublimate, 1 : 1000, but frequently some survive longer, even up to thirty minutes (Abbott). Killed in a few seconds by 3 per cent. carbolic-acid solution. Virulence variable. Pathogenic properties for animals and man have already been described. (See pp. 280, 289, 303, and the preceding section, "General Considerations concerning Pyogenic Bacteria.")

Staphylococcus Pyogenes Albus.—Cultivated by Rosenbach from pus in 1884. Differs from the aureus only by absence of pigment. As the pigment may form in aureus cultures very slowly, the cultures should be watched for several days, up to two weeks, before making a diagnosis of the albus. Pathogenic effects similar to those of the aureus, but usually the virulence of the albus is less than that of the aureus.

Staphylococcus Epidermidis Albus (Welch).—Is probably only a variety of the staphylococcus pyogenes albus. Usually grows somewhat more slowly; liquefies gelatin and coagulates milk less rapidly. Is of little virulence under ordinary conditions. Is a regular inhabitant of the epidermis, lying deeper than can be reached by disinfection of the surface of the skin. Its behavior has already been described (pp. 251, 270, and 272).

Staphylococcus Pyogenes Citreus.—Cultivated by Passet from abscesses (1885). Differs from the aureus and albus only by forming lemon-yellow pigment in the presence of free oxygen. Pathogenic effects similar to those of the aureus and albus; often of less virulence than the aureus, but may be highly virulent. Is found less frequently than the preceding staphylococci.

Staphylococci forming pigments intermediate in tint between the aureus and citreus occur, also cocci with the production of only a very faint yellowish color, perhaps produced only after prolonged growth. This has led Lubinski and others to the view that these various pyogenic staphylococci are only physiological varieties of one and the same species.

Staphylococcus Cereus Albus.—Cultivated from two abscesses by Passet (1885). Pyogenic power not considered to be demonstrated by Passet and Flügge. Levy, however, found this coccus in pure culture in abscesses and other inflammations, and produced suppuration by inoculating it into the rabbit's eye. Resembles the aureus and albus, but it does not liquefy gelatin and it forms no pigment.

The *staphylococcus cereus flavus* was isolated by Passet in pure culture from a chronic suppurative periostitis, but it does not appear to have been found again in abscesses. Passet was unable to cause abscess by inoculating it into animals. Differs from the staphylococcus cereus albus only by the formation of lemon-yellow pigment.

Streptococcus Pyogenes; Streptococcus Erysipelatos (Plate I., Fig. 3). —Observed by Ogston in pus (1881); cultivated by Fehleisen from erysipelas (1883), by Rosenbach from pus (1884). The streptococcus of erysipelas does not differ in morphology or cultural characters from the streptococcus pyogenes. The same pathogenic effects may be produced by each in animals and in man, so that the weight of evidence is in favor of the identity of the streptococcus erysipelatos with the streptococcus pyogenes, although opinions are still divided on this question.

The streptococcus pyogenes grows in chains of variable length. The individual cocci vary in size, sometimes in the same chain. They average somewhat larger than the staphylococci. In pus they occur in chains, also in pairs. Stain readily with aniline dyes and by Gram's method. Grow with or without free oxygen in all ordinary culture media. Most streptococci grow at room temperature, but more slowly than at body temperature. The streptococcus pyogenes does not liquefy gelatin, or does so slightly in some cases. Forms small, gray, granular colonies on gelatin and agar. Grows invisibly on potato, but may grow visibly. May or may not coagulate milk and cloud bouillon. Some cultures are short-lived, others may live several months. The streptococcus pyogenes may survive in dried pus for fourteen to thirty-six days. Is killed in ten minutes by exposure to 54° C. (Sternberg). Is killed in eight seconds by 3 per cent. carbolic-acid solution. Inoculated cutaneously into the rabbit's ear, virulent streptococci usually produce erysipelas, from which the animal recovers. The virulence is extremely variable, and is best tested by inoculating mice into the peritoneum, either with the first generation of a pure culture or directly with the blood or exudates containing the streptococci. Very virulent streptococci in small doses produce rapidly fatal septicæmia in mice; less virulent ones, a more or less protracted septicæmia or local inflammations; and the mouse may die after a longer or shorter period from the effects of the inoculation without the presence of streptococci at the autopsy. Streptococci are often devoid of virulence for mice. The virulence for mice does not correspond definitely to the character and severity of the streptococcus infection in the patient from whom the streptococci were obtained, although it is a general rule, with many exceptions, that the most virulent streptococci come from grave streptococcus infections in man. The pathogenic properties of streptococci for man have already been mentioned so far as they relate to surgical infections. (See pp. 258, 259, 292, and the preceding section, "General Considerations concerning Pyogenic Bacteria.")

Streptococci obtained from different sources, and even those cultivated from different cases of the same disease, vary greatly in morphology, cultural characters, and pathogenic properties. So far as virulence is concerned, this property alone cannot serve as a basis of distinction into species, as this is the most variable of all properties of pathogenic micro-organisms, and in the case of no micro-organism more variable than with the streptococcus pyogenes. The virulence of streptococci appears to vary not only in degree, but in kind, so that a streptococcus endowed with the property of producing one kind of infection—as, for example, erysipelas—may not be qualified under ordinary conditions to produce another kind of infection—as, for example, an abscess. But we observe such ready transformations in these varying degrees and qualities of virulence, and such modifications of the pathogenic effects by other circumstances than the virulence, such as the manner and site of invasion and the susceptibility of the individual, that it seems hopeless to attempt any division into physiological varieties on the basis of the quantity and quality of virulence, significant as this property is for our understanding of diverse streptococcus diseases in man.

Many attempts have been made to establish different species or varieties of streptococci on the basis of morphological, cultural, and pathogenic differences. These attempts have met with only partial success. They have tended to demonstrate the great variability of one and the same species, rather than to establish definite and constant distinctions between supposedly different species or varieties. So far, at least, as the streptococci which we ordinarily meet, and particularly those of interest for human pathology, are concerned, most authorities are of the opinion that no satisfactory division into separate species can at present be established, although it is convenient to classify streptococci according to certain prominent but varying characteristics. The characteristics which are most useful in this classification are those which appear in bouillon cultures. They are the length of the chains, the presence or absence of cloudiness of the bouillon, and the kind of sediment produced by the growth of the cocci. We thus distinguish short-chained streptococci (*streptococcus brevis*), long-chained streptococci (*streptococcus longus*), streptococci which render bouillon cloudy and those which do not, streptococci which form flocculent or sandy or scaly or viscous sediments. The name *streptococcus conglomeratus* is given to a streptococcus which grows, without clouding the bouillon, in the form of dense, separate particles, scales, or thin membranes at the bottom and sides of the tube, and on shaking the sediment it breaks up into little specks without producing uniform, diffuse cloudiness. On microscopical examination the chains in the latter case are long and interwoven in conglomerate masses. Streptococcus chains may be straight or wavy or twisted. These various distinctions are only of relative value. One form may change into another. Virulent streptococci may be found among all the groups mentioned. The streptococcus of erysipelas and most of the streptococci from abscesses and septicæmia grow in long chains in bouillon.

Micrococcus Tetragenus.—Isolated by Koch and Gaffky (1881) from phthisical cavities. Grows in tetrads enclosed in gelatinous capsules. Stains by Gram. Grows on all media at room temperature, with or

without oxygen. Forms elevated, white, non-liquefying colonies on gelatin. Pathogenic for mice, guinea-pigs, and, by intravenous and intra-peritoneal inoculation, also for rabbits. Found not infrequently in phthisical cavities and sputum, occasionally in association with pyogenic cocci in abscesses connected with carious teeth and about the neck and jaws and middle ear, rarely in abscesses elsewhere. It has been considered to be non-pathogenic for man, but it has been found in pure culture in closed abscesses in man, and Viquerat has proven experimentally that it is capable of causing suppuration in human beings. He considers that suppurations produced by the tetragenus alone are mild in character, painless, with little reaction, easily cured. Boutron proposes the name "micrococcus tetragenus septicus" for the Koch-Gaffky micrococcus to distinguish it from other similar tetragenous cocci. The latter are non-pathogenic.

Micrococcus Lanceolatus (Plate I., Fig. 5).—Synonyms: Diplococcus pneumoniæ, Pneumococcus of Fraenkel and Weichselbaum, Diplococcus lanceolatus, Micrococcus of sputum septicæmia, Micrococcus pneumoniæ cruposæ, etc. Discovered by Sternberg in his saliva in 1880. Demonstrated to be the cause of lobar pneumonia by Fraenkel and by Weichselbaum in 1886. Capsulated, lance-shaped coccus, occurring usually in pairs and short chains, sometimes in long chains. Stains by Gram. Grows best at body temperature; may grow at temperature of 18–22° C. Capable of cultivation on all ordinary alkaline media, but susceptible to slight variations in composition of culture medium. Colonies small, round, gray. Does not liquefy gelatin. Faculative anaërobe. Loses virulence and dies quickly in cultures. May survive in dried sputum or blood for four months. Killed in ten minutes at 52° C. Virulence and other properties extremely variable. Pathogenic for mice and rabbits, in less degree for guinea-pigs. Causes localized inflammations and septicæmia.

Present often in the mouth of healthy human beings (page 258). Next to the pyogenic staphylococci and streptococci, it is the most common cause of inflammations in human beings. It is probably the sole specific cause of genuine acute lobar pneumonia, and a frequent cause of bronchopneumonia, otitis media, and meningitis. With or without pneumonia it may cause inflammation in any organ or part of the body. It can produce all kinds of inflammatory exudates—serous, sero-fibrinous, purulent. It most frequently invades the body from the bronchi or lungs, sometimes from the nose, nasal sinuses, and pharynx, and occasionally from the intestine. The list of diseases which it is capable of producing is a very long one, including inflammations of any of the mucous and serous membranes, abscesses in any part of the body, mono- and polyarthritis, osteomyelitis, periostitis, parotitis, thyreoiditis, nephritis, acute ulcerative endocarditis, etc. It may cause septicæmia with single or multiple localizations. It is the most frequent cause of metapneumonic pleurisies, including empyæma. Although it may cause the gravest diseases, it is ranked as a relatively benign organism in comparison with the streptococcus pyogenes, particularly in pleurisies and suppurations. It may die quickly in inflammatory exudates, as well as in cultures, but it may also persist weeks and months.

Micrococcus Pyogenes Tenuis.—Found by Rosenbach in pus (1884).

Has been described in about twelve cases of suppurative inflammation. It is probably identical with the micrococcus lanceolatus (Neumann).

Micrococcus Gonorrhœæ or *Gonococcus* (Plate I., Fig. 4).—Discovered by Neisser in gonorrhœal pus in 1879. First cultivated by Bumm in 1885 on human blood-serum. Found constantly in gonorrhœal pus. The cocci are in pairs, with the adjacent sides flattened against each other, with a clear interspace (biscuit shape). Groups of four with adjacent sides flattened also occur. Particularly characteristic is the inclusion of the cocci within leucocytes, but they occur also free and attached to epithelial cells. Of diagnostic importance is failure to stain by Gram, which distinguishes the gonococcus from all the preceding cocci, but not from the so-called pseudo-gonococci (pp. 266 and 267). Facultative anaërobe. Grows only at body temperature or neighboring temperature. Does not grow on nutrient gelatin or plain agar, or on the latter only with difficulty and occasionally. Grows best on a mixture of human blood-serum and nutrient agar (one to two or three parts) (Wertheim). The addition of sterile human urine improves the serum-agar mixture (Steinschneider). Surface colonies pale, grayish, translucent, finely granular, with finely notched borders. Forms a membrane in bouillon and blood-serum mixed, leaving the fluid clear. Cultures on serum-agar when prevented from drying may live forty-five days. Inoculation of pure cultures into healthy human urethræ produces typical gonorrhœa. The gonococcus is a strict human parasite. It dies quickly in dried pus outside of the body. Virulence soon disappears, as a rule, in artificial cultures.

The gonococcus is in general non-pathogenic for animals, but when inoculated with bits of agar into the eye or into the peritoneal cavity of mice and guinea-pigs it may cause suppurative inflammation. In human beings its growth is usually superficial, and by preference on mucous membranes covered by cylindrical or transitional epithelium, but it may grow down deeply into connective tissue and between muscle-fibres, and may attack mucous membranes covered by flat epithelium. It is the cause of most cases of salpingitis, pyosalpinx, and the accompanying peritonitis. It may produce genuine abscesses (ovarian, peri-urethral). It may be conveyed by the blood-current and cause inflammations in distant parts, most commonly arthritis, also endocarditis, pericarditis, pleurisy, and myocarditis. Every condition of rigid proof of the causation of arthritis by the gonococcus (exclusive presence, isolation in pure culture, and experimental production of gonorrhœa by inoculation) has been fulfilled. It is the usual cause of gonorrhœal rheumatism. All of these conditions, complicating gonorrhœa, may, however, be produced by other invading micro-organisms or be mixed infections with the gonococcus.

Bacillus Pneumoniæ of Friedländer (Pneumo-bacillus or Pneumococcus of Friedländer).—Isolated by Friedländer in 1883 from croupous pneumonia. Short, plump rods with rounded ends provided with distinct capsules in the animal body. Does not stain by Gram. Facultative anaërobe. Grows at room temperature. Forms prominent, opaque-white, non-liquefying colonies on gelatin. Grows on all media. Ferments glucose and lactose and produces gas-bubbles on potato. Pathogenic for mice, less so for guinea-pigs, and still less so for rabbits, which, however, may become infected by intra-peritoneal inoculation. Found occasionally

in the healthy human mouth and nose, also outside of the body. It is found most frequently in inflammations of the mouth, nose, and middle ear. It may cause broncho-pneumonia, and has been observed in a very few cases of empyæma and of meningitis secondary to middle-ear disease and to injury. It is a rare organism in this country.

The *bacillus of rhinoscleroma* resembles closely the Friedländer bacillus, and, according to some, there is no reliable differential character, not even the greater resistance to decolorization by Gram's method, which has been the point chiefly emphasized. There is a group of capsulated bacilli, resembling the Friedländer bacillus, some from human beings, others from animals, which have not been satisfactorily differentiated from each other (see page 262).

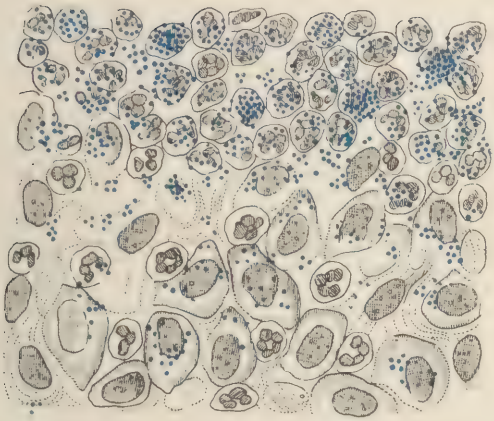
Bacillus Pyocyaneus (Plate I., Fig. 2).—First cultivated by Gessard from blue pus (1882). A slender, motile, liquefying bacillus, decolorized by Gram, growing rapidly, even at ordinary temperatures, in all culture media. In the presence of oxygen forms bluish, fluorescent green and a whole scale of pigments. Interesting modifications of character, especially as to color production, can be produced artificially, and are observed under natural conditions, constituting, according to some writers, distinct varieties of the bacillus. Is widely distributed, occurring often on the human skin, in the fæces, and outside of the body. In wounds stains the dressings bluish green, and produces a somewhat characteristic offensive odor. Increases suppuration of wounds, usually with little constitutional disturbance. Pathogenic for animals. Is found not infrequently in perforative peritonitis and appendicitis, sometimes in phlegmons, otitis media, broncho-pneumonia, and inflammations of serous membranes, associated usually with other bacteria. It was found by Ernst in tuberculous pericarditis (Plate I., Fig. 2). Often found in diarrhœal and dysenteric discharges. May cause general infections in human beings. With or without general infection it may cause hemorrhagic and necrotic enteritis, a form of pyocyaneus infection in human beings which we have repeatedly observed at autopsy. Instances of invasion of the body from wounds by the bacillus pyocyaneus have not been observed.

Bacillus Pyogenes Fœtidus.—First cultivated by Passet from stinking pus of a perirectal abscess (1885). Short bacilli with rounded ends. Cultures have a foul odor; in other respects they do not appear to differ from those of the bacillus coli communis. This bacillus probably belongs to the group of colon bacilli. It has been found in pure culture in closed abscesses, but more frequently is associated with other bacteria.

Bacillus Coli Communis.—Isolated by Escherich from fæces of infants (1886). There is a group of bacilli, called the colon group, presenting similar characters, but with much variation in their cultural and other properties. Short rods with rounded ends, also longer forms. Either motile or non-motile. Do not stain by Gram in cultures or in the tissues, but do in normal stools. Grow at low as well as high temperatures on all media. Facultative anaërobes. Form large, spreading, grayish-white, non-liquefying colonies with notched borders on gelatin and agar, sometimes circumscribed, round, white colonies. On potato, brownish, yellowish, white, or even scarcely visible growth. Coagulate milk, ferment glucose, lactose, and maltose. Constant inhabitants of the intestine, also widely

PLATE I.

FIG. 1.



Section through wall of abscess showing staphylococcus pyogenes aureus (p. 315). BAUMGARTEN.

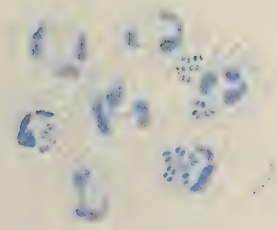
FIG. 2.

Cover-glass preparation of pericardial exudate showing bacillus pyocyaneus stained blue, and the tubercle bacillus stained red (p. 320). ERNST.

FIG. 3.

Streptococcus pyogenes; streptococcus erysipelatos (p. 316). PRUDDEN.

FIG. 4.



Micrococcus gonorrhœæ or gonococcus (p. 319). ABBOTT.

FIG. 5.

Micrococcus Lanceolatus (p. 318). ABBOTT.

distributed in external nature. The colon bacillus is a frequent invader of the internal organs in all sorts of diseases, especially when there are intestinal lesions. It manifests no evident pathogenic action in most of these cases, and is then without clinical significance. It occurs frequently associated with other bacteria in infected wounds and other inflammations of exposed surfaces. Here also it does not usually appear to cause serious disturbance. The fact that the colon bacillus is so common and widely distributed, and found so often as a harmless invader, should lead to much caution in interpreting the significance of its presence when it occurs in definite lesions. There is no doubt, however, that it may be pathogenic for man. It plays an important rôle in inflammations of the urinary tract and biliary passages; also, but usually with less independence, in peritonitis and appendicitis. The list of diseases in which it may be found is a very long one, and includes inflammations in all organs and parts of the body. Attention has already been called to its pathogenic properties for man (page 274). In general these properties are of a mild character. One of its leading rôles is to invade territory already occupied by other bacteria or previously damaged. It may be concerned in the production of gall-stones, in the interior of which it has been found by the writer with great frequency. Its virulence as tested upon animals is variable, but is generally manifest only after inoculation of large doses, which kill by intoxication rather than infection.

Bacillus lactis aërogenes is described by Escherich as shorter and plumper than the colon bacillus. Forms more circumscribed, elevated, white colonies, and coagulates milk and produces gas on potato more quickly and energetically than the latter. Predominates in the upper part of the small intestine. Of late most writers include this bacillus in the colon group, with which it corresponds in its general pathogenic characters. It is sometimes described as an opaque variety of the colon bacillus.

Bacillus Typhi Abdominalis.—Mention is made of this bacillus, which is chiefly of medical interest, not to describe its characters, but to call attention to its capacity in rare instances to produce genuine suppurative inflammations in man, and especially to cause periostitis and osteomyelitis as a sequel of typhoid fever. Most suppurations accompanying or following typhoid fever are due to the pyogenic cocci or are mixed infections, but the typhoid bacillus may occur alone in abscesses. The most common post-typhoid osseous affection is periostitis with cortical ostitis. The exudate, when caused by the typhoid bacillus alone, may be dark and thin with much detritus, or syrupy in consistence, or genuine pus. The affection is oftener in the ribs than elsewhere, and may be obstinate toward treatment. It may develop several months, and it has been claimed even years, after typhoid fever. Some observations indicate that the typhoid bacillus may cause meningitis and inflammations of serous membranes.

Bacillus Proteus.—In 1885, Hauser isolated from putrefying substances the rapidly-liquefying *proteus vulgaris*, the slowly-liquefying *proteus mirabilis*, and the non-liquefying *proteus Zenkeri*, which he originally supposed to be three distinct species, but which he now regards on satisfactory evidence as three varieties of the same species, called bacillus proteus. The main characters of this bacillus are its

pleomorphism, and especially moving, wandering, irregular projections and islands from its colonies on gelatin and agar (swarming colonies). It is motile. This is one of the most widely-distributed bacteria, and is concerned in the decomposition of animal and vegetable material. It is not uncommon in the intestinal contents. Although repeatedly observed in inflammations of exposed surfaces, in appendicitis, in perforative peritonitis, and even in closed abscesses in association with other bacteria, it has been generally considered to be non-pathogenic for man, but our autopsy material has convinced us that it may be pathogenic. It may be unassociated with other bacteria in abscesses and in peritonitis, and it may cause general infection by invading the blood and internal organs (Flexner). In moderate and large doses it is pathogenic for animals.

Bacillus Œdematis Maligni.—Long spore-forming bacillus resembling the anthrax bacillus, but narrower and with rounded ends. Forms long threads. Strict anaërobe. Liquefies gelatin with gas-production and foul odor. Widely distributed in the soil and in the fæces of animals. Pathogenic for animals. No instance is recorded of infection of a previously healthy person with this bacillus, but Brieger and Ehrlich have reported two cases of malignant œdema following the hypodermic injection of musk in a typhoid patient. The bacilli were accidentally introduced by the syringe.

Bacillus Aërogenes Capsulatus; Bacillus Phlegmones Emphysematosæ.—An anaërobic bacillus first described by Welch and Nuttall in 1892 as the cause of rapid formation of gas in the blood-vessels and organs after death. Capsulated thick bacillus, averaging 3 to 6 μ in length. Readily stained by aniline dyes, including Gram's stain. Grows slowly at room temperature, best at body temperature. Produces gas abundantly in all media containing fermentable substances. Does not form spores. When injected subcutaneously or intravenously into animals which are killed shortly afterward, it develops rapidly, with abundant formation of gas throughout the body. The gas is odorless and burns with a blue flame. There is at first no putrefactive decomposition. In the first case reported by Welch and Nuttall the autopsy was made eight hours after death in cool weather, and gas was abundant in the blood-vessels and liver. This bacillus is doubtless the cause of the gas-formation in many cases reported as death from the entrance of air into the veins, especially from the uterus after abortion, as was proven to be true in a case reported by Graham, Steward, and Baldwin, and in two cases reported by P. Ernst. This bacillus was found in a case of emphysematous gangrene of the hand reported by Mann. It is probably identical with the bacillus found by E. Fraenkel in four cases of emphysematous phlegmon reported in 1893, and called by him *bacillus phlegmones emphysematosæ.* It has been found by the writer in three cases of perforative peritonitis. It may cause emphysema of the subperitoneal tissues. It is probably a rather widely distributed bacillus.

Bacillus Diphtheriæ.—Observed by Klebs (1883), first cultivated and accurately described by Löffler (1884). Straight or slightly curved rods, averaging 1.2 to 2.5 μ in length, characterized especially by irregularities in shape and staining. Particularly characteristic are swollen ends and deeply-staining chromatin-granules in the bacilli. Stains by

Gram. Not motile. Does not form spores. Facultative anaërobe. Optimum temperature for growth 33–37° C. Grows only slowly and slightly, if at all, below 20° C. Grows on all alkaline culture media, invisibly on potato, best on Löffler's blood-serum bouillon mixture. Does not liquefy gelatin. Forms on agar grayish-white, granular colonies with slightly irregular margins. In bouillon grows in the form of small grayish particles, with or without clouding of the medium, often with formation of surface membrane. Particularly important as a diagnostic criterion is the change of the alkaline to acid reaction by forty-eight hours' growth in bouillon containing carbohydrate. Thermal death-point, 58° C. in ten minutes. May survive in some culture media eighteen months, but may die in three or four weeks. Lives longer in the dark than when exposed to light. Resistant to desiccation. May survive for three to five months in dry membranes, but usually dies sooner. Cultures dried on threads survive three to four weeks at room temperature. Both virulent and non-virulent diphtheria bacilli occur, the latter rarely in diphtheria. Pathogenic for many animals, and especially for guinea-pigs. By subcutaneous inoculation there is produced extensive local inflammation and necrosis. The animal dies usually in thirty-six to sixty hours, with necrotic foci in various internal organs and serous transudates in the serous cavities. The bacilli are found only near the seat of inoculation or in very small number in the organs. With less virulent cultures or smaller doses subacute and chronic infections or intoxications ensue. Genuine pseudo-membranes, as a rule with little tendency to spread, follow inoculation of mucous membranes superficially injured. The virulent diphtheria bacillus produces by its growth in cultures or in the animal body a powerful poison, called the toxin or toxalbumin of diphtheria, to which the constitutional symptoms, the lesions of internal organs, and the paralysis are due.

The diphtheria bacillus is the cause of all cases of genuine diphtheria. Similar pseudo-membranous inflammations of the throat and air-passages may be caused by streptococci. The intensity of the affection caused by the diphtheria bacillus varies from a slight inflammation without false membrane to the gravest pseudo-membranous inflammations.

The diphtheria bacillus is incapable of attacking the intact skin. It may, however, produce pseudo-membranous inflammations on excoriated, ulcerated, and wounded skin. Neisser has reported the case of a child five and a half years old with diphtheria of the throat in whom thick, firmly-adherent pseudo-membrane covered the skin about the anus over a space 10 cm. long and 4 cm. broad. There was œdema of the scrotum and penis. Löffler bacilli were found in the false membrane and throughout the infiltrated corium. The localization of the diphtheria bacillus in cutaneous surfaces which have been deprived of the epithelial covering by excoriation, eczema, ulceration, herpes, wounds, has been observed many times in persons affected with diphtheria of the throat, although it is not common. This localization may be attended by a pseudo-membrane, or by simple superficial necrosis, or by ordinary suppuration or inflammation in no way suggesting diphtheritis. Park found diphtheria bacilli in two cases in wounds of the finger received by physicians in intubating children with diphtheria. They persisted for six weeks in one case. Wright has demonstrated the presence of this bacillus in

excoriated or ulcerated surfaces of the skin in 7 cases, in paronychia in 1, in mastoid abscess in 1, in purulent conjunctivitis in 1,—all in cases of diphtheria. The diphtheritic process may extend by continuity to a tracheotomy wound. More frequently the wound is unaffected, even in cases where the diphtheria bacillus may be demonstrated upon its surface. Extensive necrotic and septic involvement of tracheotomy wounds is more frequently due to streptococci, with or without association with the diphtheria bacillus, than to the latter micro-organism alone. Brunner has reported three cases of infection of wounds with the diphtheria bacillus in association with pyogenic cocci in persons without demonstrable connection with other cases of diphtheria and without any affection of the throat. In only one case was there pseudo-membrane. The presence of the diphtheria bacillus was not suspected in any of these cases before the bacteriological examination.

In this connection a few words may be said regarding the general subject of wound diphtheritis, concerning which much confusion exists. Here, as well as in diphtheritis of mucous membrane, it is important to bear in mind that the term "diphtheritis" is a purely anatomical one, and implies nothing as to the causation of the affection. The term "diphtheria," on the other hand, should be restricted to the affection caused by the Löffler bacillus wherever this may be localized. There are three anatomical conditions of a wound to which the epithet "diphtheritic" has been applied—namely, first, the presence of an adherent fibrinous false membrane incorporated with underlying necrosis of the tissues; second, the presence of a fibrinous pseudo-membrane loosely attached to the underlying tissues, which may present no distinctive alteration; and, third, more or less extensive necrosis of the tissues of the wound without a distinct false membrane. Only the first condition is properly called diphtheritis; the second may be called simple pseudo-membranous or croupous inflammation, and the third is necrotic inflammation.

Wound diphtheria is infection of a wound by the Löffler bacillus. It may or may not be wound diphtheritis in the anatomical sense. Wound diphtheria may manifest itself as a simple inflammation, or inflammation with superficial necrosis, or inflammation with more or less adherent pseudo-membrane. Pyogenic cocci are usually associated with the Löffler bacillus in the diphtheria of wounds. Paralysis may follow wound diphtheria. As the same anatomical conditions in a wound may be produced by various causes, a positive diagnosis of wound diphtheria can be made only by bacteriological examination. The conditions as regards varying intensity and character of the infection, association with other bacteria, particularly streptococci, and the necessity of a bacteriological examination to establish the diagnosis, are in no way different in the diphtheria of wounds from those in diphtheria of mucous membranes. As has already been stated, wound diphtheria may occur without demonstrable connection with cases of diphtheria and without affection of the throat in the individual attacked, but such occurrences are rare.

Diphtheritic, necrotic, and croupous inflammations of wounds are caused most frequently by other micro-organisms than the Löffler bacillus. Here, as with similar inflammations of mucous membranes,

the streptococcus pyogenes appears to be an important causative agent, so far as can be judged from the small number of cases hitherto examined bacteriologically. In this comparatively rare class of streptococcus infection of wounds the intensity and extent of the inflammation vary within wide limits.

It is not, or formerly was not, a particularly rare occurrence for coherent false membranes to develop upon granulating surfaces without notable disturbance in the process of repair and without constitutional disturbance. The membrane in these cases can be readily stripped off, after which another membrane is likely to form. It has been proposed to call this relatively inoffensive wound complication "wound croup," in distinction from the more severe wound diphtheritis. In two cases of croupous membranes on granulations Brunner found the streptococcus pyogenes in pure culture. In similar cases he and Tavel have found also the bacillus coli communis in pure culture. The condition may doubtless be associated with the presence of various micro-organisms, and is not, therefore, a specific one. In croupous inflammations of fresh wounds Brunner found the streptococcus pyogenes in association with other pyogenic cocci.

How much the development of diphtheritic and necrotic inflammations of wounds is influenced by the general condition of the patient is shown by the greater frequency of its occurrence in persons prostrated with typhoid fever, scarlet fever, septicæmia, pyæmia, and other debilitating causes.

Diphtheritic inflammation of operative wounds involving the mouth and the bladder is more common than a similar affection of wounds in other parts of the body. The Löffler bacillus is not concerned, as a rule, with diphtheritis of these wounds, any more than it is with diphtheritic cystitis or enteritis.

Much interest attaches to the question of the causation of hospital gangrene, that frightful scourge of pre-antiseptic surgery in crowded hospitals, particularly in military hospitals. Hospital gangrene has been designated "wound diphtheritis," but it differs from the necrotic and diphtheritic inflammations of wounds, which are now occasionally observed, in many features, particularly by its phagedenic character and its mortality. It has apparently disappeared, at least from civilized countries, and there has been, therefore, no opportunity to make a bacteriological examination by modern methods of any case of this disease. Although some of the older writers identified the cause of hospital gangrene with that of true diphtheria, it seems, with our present knowledge, highly improbable that this is true. Our observations of the effects produced by the diphtheria bacillus with or without association with other bacteria in wounds do not indicate that this organism can have played any essential rôle in the causation of hospital gangrene. Some authorities are of the opinion that hospital gangrene is a specific infection due to a specific micro-organism which has disappeared from civilized countries, as the micro-organism of the plague has disappeared. It seems to the writer more probable that it was due to pyogenic bacteria which still exist, but which under the special conditions prevailing where hospital gangrene occurred had acquired a degree and kind of virulence with which we are no longer familiar. Thanks to antiseptic

surgery, these special conditions are not likely to be repeated in civilized countries.

Bacillus Tetani.—Observed by Nicolaier (1884) in wounds in cases of tetanus and demonstrated in garden earth, first obtained in pure culture by Kitasato (1889). Slender, straight bacilli, varying in length from short rods to long threads. Sluggishly motile. Spherical spores, thicker than the rods, develop at one end of the bacilli, giving them a drumstick or pin shape. Stains by Gram. Anaërobic. Grows best at body temperature, slowly at 18–20° C., not at all below 14° C. Spores are formed in cultures at body temperature in thirty hours, in cultures at 20° to 25° C, not until after a week. Grows in nutrient gelatin, which is slowly liquefied with slight gas production; in agar and bouillon when free oxygen is excluded. Growth in gelatin is fuzzy, radiating, like a thistle. Dried spores live months and years. Cultures containing spores dried on silk threads were found alive after several months by Kitasato. Henrijean demonstrated living, virulent tetanus spores on a piece of wood which had been extracted eleven years previously from the wound in a boy with fatal tetanus. The spores are killed in five minutes by moist heat at 100° C. They withstand in the moist condition for an hour a temperature of 80° C.—a property which was utilized by Kitasato to destroy other bacteria in obtaining pure cultures of the tetanus bacillus. The spores survive and preserve their virulence for ten hours in 5 per cent. carbolic acid; they are killed in fifteen hours. They are not killed by putrefactive bacteria.

The tetanus bacillus is more or less pathogenic for nearly all warm-blooded and some cold-blooded animals. Infection takes place only through a wound. The period of incubation varies from a few hours to several days, according to the susceptibility of the animal and the dose. Experimental tetanus corresponds in all essential particulars to human tetanus. Tetanic spasm appears first in the muscles nearest the seat of inoculation.

Tetanus is a toxic infection. The bacilli multiply only in the immediate neighborhood of the wound, and do not invade the blood and organs. Inoculation with pure cultures is a pure intoxication as a rule, with but little multiplication of the bacilli, so that at the autopsy it may be difficult to find any bacilli. When impure cultures and foreign bodies are introduced into the wound the bacilli are more readily demonstrable at autopsy. There are no demonstrable lesions of internal organs in experimental tetanus.

All of the symptoms of tetanus can be produced by the germ-free filtrate of tetanus cultures. It is the only infectious disease known every feature of which can be produced experimentally by injection of the poison without the micro-organisms. In the case of diphtheria all of the symptoms and lesions can be produced by the poison except the local false membrane. This requires the presence of the bacilli.

Brieger found in impure tetanus cultures four crystallizable alkaloidal substances belonging to the class of ptomaïnes. Three of these he called tetanin, tetanotoxin, and spasmotoxin. He found also an unnamed base. As these ptomaïnes produced spasms by injection into animals, this result was at first thought to indicate that the poison of tetanus had been isolated in a state of chemical purity. Subsequent investigations have

shown that these ptomaïnes do not reproduce all of the characteristic symptoms of tetanus. They are not the real tetanus poison, and no particular interest any longer attaches to them.

The real poison of tetanus belongs to a different class of substances—namely, the so-called toxic proteids or toxalbumins, substances about which we know very little chemically, but a great deal physiologically. We do not even know positively that the tetanus toxin is a proteid, but it is generally assumed to be. To this same class of substances belong the toxin of diphtheria, the venom of snakes, and certain poisonous substances produced by vegetable cells, as ricin, abrin, robin.

The specific tetanus toxin has been demonstrated both in cultures of the tetanus bacillus and in the bodies of animals. It has been found in the blood both during life and after death. It does not appear to be eliminated in appreciable amount by the urine unless very large doses are given. According to Kitasato, the poison is destroyed in the presence of water in five minutes at 65° C., in one and a half hours at 55° C; it stands drying at ordinary temperatures; is not injured by dilution with water or bouillon; is sensitive to acids and alkalies. It is destroyed by the acid gastric juice. It is injured by exposure to light. So sensitive is the tetanus poison to chemical reagents that Kitasato was unable to find any means of obtaining the poison in a condition approaching purity, and he expressed ignorance as to its real nature. Brieger and Cohn have, however, been more successful, and have isolated a substance possessing the properties of the tetanus poison in a condition approaching purity. As this substance was found to be without most of the proteid reactions, they consider that it is not an albumin in the ordinary sense of that term.

The tetanus toxin is of appalling potency. Kitasato obtained liquid cultures of such virulence that 0.00001 ccm. of the germ-free filtrate, corresponding to 0.00023 mgm. of the dried filtrate, sufficed to kill a mouse with tetanus. Of course only a part of the dried substance is the real poison. Of the purified substance obtained by Brieger and Cohn, who had at their disposal cultures of less primary virulence than those of Kitasato, 0.000,000,05 grm. killed a mouse of 15 grm. weight. As the fatal dose of the tetanus poison increases with much regularity in proportion to the weight of the animal, this would represent 0.23 mgm. as the fatal dose for a man weighing 70 kilo. When it is considered that the minimal fatal dose of atropine for an adult is 130 mgm. and of strychnine is 30–100 mgm., some conception of the terrible energy of this bacterial weapon can be obtained. The substance separated by Brieger and Cohn was not in a state of chemical purity. The tetanus poison, like the diphtheria poison, does not cause symptoms immediately after its introduction. With small doses it may be days before recognizable symptoms appear. This behavior is unlike that which we are accustomed to attribute to chemical poisons, and raises the question whether the poison may not be reproduced in the body, or whether the substance injected is itself the poison, and may not be in the nature of an enzyme which leads to the production of the real poison within the body. These questions cannot at present be answered.

An interesting example of the effect of the pure tetanus toxin upon man is reported by Nicolar. In working with the filtrate of a tetanus

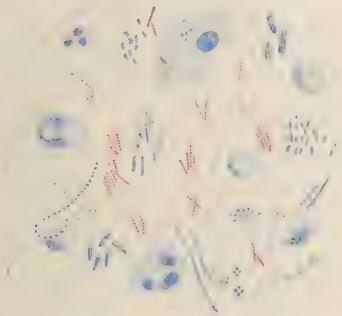
culture he accidentally stuck the point of the needle of a hypodermic syringe containing some of the fluid into his left hand. Only the moisture adhering to the needle was introduced into the puncture. After three and a half days the first symptoms of tetanus were manifested by contracture of the left thumb. There followed in succession contraction of the hand, the arm, then trismus, opisthotonos, general contractures, and convulsions. The treatment was by large doses of chloral. After three weeks improvement began, and recovery was complete after forty-one days. In this unique case the tetanus toxin was introduced in minimal amount without the bacilli. Nicolar, in view of the fact that no symptoms were manifested until the third day, adopts the view that the culture fluid does not contain the real poison, but produces it by a kind of fermentation after introduction into the body.

The distribution of the tetanus bacillus and the factors favoring infection with tetanus have already been described (pp. 253, 265, 276, and 289).

Susceptible animals may be rendered immune from tetanus by the injection of the tetanus poison, at first weakened by chemical agents or heat, and then administered in full strength in constantly increasing doses. This is antitoxic immunity, already described, which has nothing to do with natural immunity. The hen is naturally immune from tetanus, but not by virtue of any antitoxic power of the blood. The blood-serum and other fluids of animals rendered artificially immune from tetanus are capable, by virtue of their antitoxin, of rendering susceptible animals resistant to tetanus (passive immunity), or even of preventing the development of the disease or of curing the disease after reception of the virus. Behring in 1892 reported that in the course of two years he had by successive injection of increasing doses of the tetanus toxin rendered a horse so highly immune that the immunizing value of its blood-serum was 1 to 10,000,000, by which is meant that $\frac{1}{10000000}$th ccm. of serum will protect 1 grm. weight of mouse from the effects of the subsequent injection of the smallest fatal dose of the tetanus poison, or 1 ccm. of serum suffices to immunize 500,000 mice, weighing each 20 grams, or 200 sheep, weighing each 50 kilo. When, however, the attempt is made to prevent the development of the disease immediately after the reception of the virus, a larger quantity of the serum is required to afford protection than a few hours previously, and as time elapses the amount of serum required rapidly increases, until, as soon as the very first symptoms of the minimal fatal dose of tetanus poison appear in the mouse, one thousand times the quantity of serum necessary for simple preventive immunization must be injected. After twenty-four hours the necessary quantity of serum possessing an immunizing value of 1 to 1,000,000 is too great to be introduced into the animal. To produce the same curative effects in large animals as in small it is necessary to inject proportionately larger amounts, the dose being in approximately direct ratio to the respective weights of the animals. These considerations manifestly suggest serious difficulties in the application of the antitoxic treatment of tetanus to human beings. But there is another difficulty of probably greater force—namely, that we have no indication that tetanus will result from a wound in man until characteristic symptoms have appeared. By that time tetanus poison has accumulated in considerable amount in the system. Kitasato was unable to prevent the development of tetanus in mice by the com-

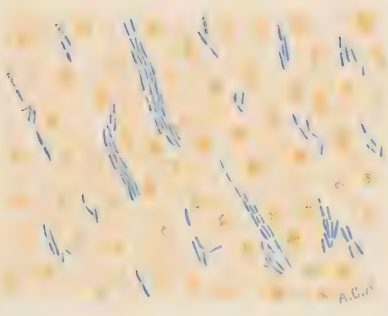
PLATE II.

FIG. 1.



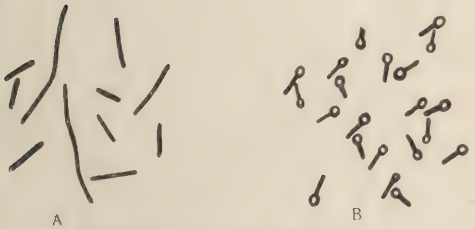
Tubercle bacillus and streptococci in sputum (p. 329). ABBOTT.

FIG. 2.



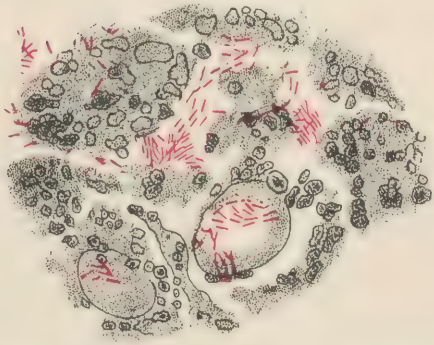
Anthrax bacillus in section of liver of mouse (p. 331). ABBOTT.

FIG. 3.



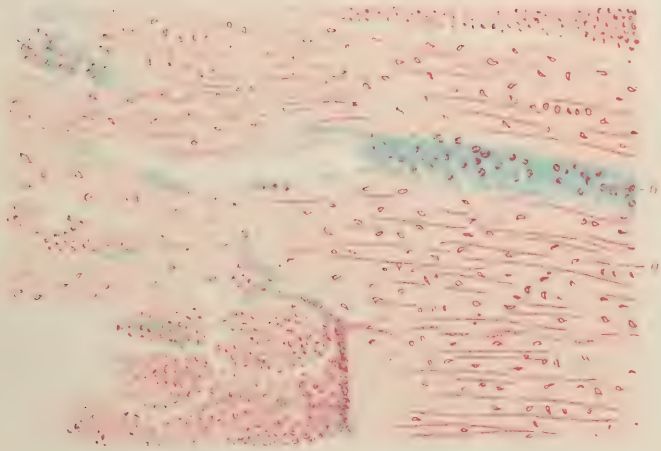
Tetanus bacillus (p. 326). ABBOTT.

FIG. 4.



Section of glanders nodule, showing glanders bacilli (p. 330). FLÜGGE.

FIG. 5.



Longitudinal section of rabbit's tibia showing osteomyelitis produced by intravenous injection of the staphylococcus pyogenes aureus. The cocci are colored blue. *a*, Compact tissue of bone; *b*, Haversian canal filled with staphylococci (p. 315). LANNELONGUE and ACHARD.

plete excision and thorough cauterization of the wound one hour after inoculation with tetanus bacilli. It is not positively proven that curative antitoxic serum neutralizes poison which has already been received into the system before injection of the serum, although it is capable of neutralizing poison formed after its administration. We stand in a much less favorable position for the successful treatment of human tetanus by antitoxin than is the case with diphtheria, where the conditions are more favorable both as regards progressive increase of dosage in proportion to the weight, and especially as regards the possibility of beginning treatment before the absorption of large quantities of the poison. These are the scientific considerations relating to the treatment of tetanus by antitoxin. Its practical application and the results of treatment in human beings belong to the article on Tetanus in this work.

Bacillus Tuberculosis.—Discovered and first cultivated by Koch (1882), independently and at about the same time demonstrated microscopically in tubercles by Baumgarten. Slender, straight, or slightly curved or bent, non-motile rods, 1.5 to 4 μ in length, which averages five to six times the breadth. In unstained specimens glistening dots, in stained specimens clear spots, are often seen in the rods, which thereby present a beaded appearance. These are interpreted by Koch and others as spores, but this has not been proven. No greater resistance to heat and other injurious agencies has been demonstrated for bacilli containing these suspected spores than for bacilli without them. Tubercle bacilli take up staining dyes with difficulty, but when once thoroughly stained by intense aniline dyes they retain the color after it has been extracted by acids, alcohol, and other decolorizers from all other known bacteria except the leprosy bacillus and some examples of smegma bacilli. (See p. 254.) It is by this peculiar staining reaction that tubercle bacilli are differentiated from other bacteria. The tubercle bacillus grows best in the presence of free oxygen, but is capable of growth without free oxygen. Optimum temperature for growth, 37 to 39° C. Does not grow below 29° C. Was first cultivated by Koch on solidified cow's blood-serum; has since been cultivated on potato, and on nutrient agar and bouillon to which 5 to 6 per cent. glycerin has been added. On blood-serum the growth first becomes visible after ten to fourteen days. It forms dry, lustreless, compact white scales, loosely attached to the surface. By coalescence of the colonies extensive membranous growths are formed. Grows in the form of a membrane on the surface of fluid media, without clouding the fluid. The tubercle bacillus is the most resistant to heat of all pathogenic bacteria not positively proven to form spores. The statements of different experimenters as to its thermal death-point are so widely divergent that bacilli from different sources, or at least under different conditions, would seem to vary in this respect; but it is more probable that the discordant results are due to failure to ensure exposure of the bacilli to the actual temperature of the surrounding fluid. The physical conditions as regards distribution of the temperature in heated animal fluids, culture media, etc., especially when solid masses are present, are not of so simple a nature as many of the experimenters upon the subject of the thermal death-point of bacteria seem to suppose. According to the careful experiments of Forster, tubercle bacilli are killed, or at least are rendered incapable of infecting guinea-

pigs, by ten minutes' exposure to a temperature of 70° C and by one hour's exposure to 60° C. They were not killed in forty-five minutes by heating to 60° C. They are surely killed in a few minutes by the boiling temperature. They retain their vitality in dried sputum for nine or ten months, but at the last with some loss of virulence. They resist putrefaction for a considerable time. They are killed in sputum by 3 per cent. carbolic acid in twenty hours; they are killed in a few minutes by 3 to 5 per cent. carbolic acid when the acid can come into direct contact with the bacilli. They resist the action of the gastric juice. When exposed in thin layer to the direct action of the sun's rays they are killed in a few minutes—much more slowly when in a thick layer.

The tubercle bacillus is a strict parasite, incapable under ordinary conditions of multiplication in the outer world, but capable of prolonged survival outside of the body. It is the sole cause of tuberculosis. The pathogenic manifestations of the tubercle bacillus have been described by Dr. Councilman (p. 239), and will be further considered in the articles treating of the various forms of surgical tuberculosis.

The bacillus of avian tuberculosis is a different species, or at least a different variety, from that of human tuberculosis.

Bacillus Lepræ.—Discovered by Hansen (1879) in leprous tubercles. Morphologically, the leprosy bacillus resembles very closely the tubercle bacillus, from which it probably cannot be distinguished in size and shape. It presents clear, unstained dots like those observed in tubercle bacilli. It resembles the tubercle bacillus also in its staining reactions, the only important difference being that it is more readily stained by aniline dyes than the tubercle bacillus. It stains well by Gram's and Weigert's fibrin stain. It is non-motile. Although many observers claim to have cultivated the leprosy bacillus, none of these claims have been established, at least not to the satisfaction of most bacteriologists. Most experimenters have had only negative results from the inoculation of leprous material into animals. The positive results reported by Damsch, Vossius and Melcher, and Ortman are open to criticism in their interpretation. The apparently successful inoculation of a condemned criminal in the Sandwich Islands by Arning has also been criticised as not conclusive. The constant and exclusive presence of the bacillus lepræ in leprosy cannot be reasonably interpreted otherwise than that the bacillus is the cause of the disease. The characteristic bacilli are present in enormous number in the leprous nodules, being chiefly enclosed within cells. They have also been found in the lesions of the disease in all parts of the body. They are very rarely in the blood.

Bacillus Mallei.—Discovered by Löffler and Schütz (1882) in the lesions of glanders. Somewhat shorter and thicker than the tubercle bacillus. Presents often clear, unstained spaces in the rods. It probably does not form spores. Decolorized by Gram. Stains with the usual aniline dyes, but is so easily decolorized that its demonstration in sections is somewhat difficult. Like the typhoid bacillus, it occurs in the tissues especially in clumps. Non-motile. Facultative anaërobe. Grows best at body temperature, but is capable of growth at room temperature. Grows on all culture media, but, as has been shown by Theobald Smith, far better on acid (non-neutralized) than on alkaline media. Particularly characteristic is the growth on potato, on which the glanders bacillus

forms at first a translucent, amber-yellow layer, later a reddish-brown layer with discoloration of the potato. Growth on agar whitish, moist; if the medium be acid, thick and abundant. The virulence diminishes in successive generations in artificial cultures. The glanders bacillus may survive in the dried condition for three and a half months, but usually dies within two or three weeks. There are observations which indicate that it may survive for at least a year and a half in unoccupied, infected stables. By inoculation of horses with pure cultures glanders is produced. The bacillus is pathogenic for several species of animals. The guinea-pig and the field-mouse are particularly susceptible. White mice are resistant. The field-mouse dies from experimental inoculation usually in three or four days with acute infection and minute tubercle-like nodules in the spleen and liver. The lesions in the guinea-pig are most characteristic, consisting in a caseous ulceration at the seat of subcutaneous inoculation, which, however, is often absent; swelling and necrotic suppuration of the testicles; swelling and ulceration of the joints; and nodules in the spleen and liver, sometimes elsewhere. The best method of diagnosing a suspected case of glanders is to inoculate the material into the peritoneal cavity of a male guinea-pig. In four or five days, at the most in eight or ten days, the characteristic swelling and inflammation of the testicles can be detected. The bacilli are in the lesions, but scanty or absent in the blood. Mallein is a product derived from cultures of the glanders bacillus, and is analogous in its properties and uses to tuberculin derived from the tubercle bacillus. It is used for the diagnosis of glanders in animals, as tuberculin is used for the diagnosis of tuberculosis.

Bacillus Anthracis.—Discovered in the blood of animals affected with anthrax by Pollender (1849); also observed by Davaine (1850), Rayer (1851), and Brauell (1857). The studies upon the anthrax bacillus laid the foundation-stone of modern bacteriology. The bacillus is 1 to 1.5 μ broad and 3 to 10 μ long. It grows out into long threads made up of bacilli, the adjacent ends of which are sharply cut and slightly concave. Not motile. Stains readily with aniline dyes, including Gram's stain. Forms spores in the presence of oxygen, but never within the animal body. Grows at room temperature, best at body temperature; does not grow below 12° C. Grows on all culture media. Liquefies gelatin with moderate rapidity. Colonies on gelatin are whitish, often with fuzzy, irregular, hair-like projections. Similar bristle-like projections often characterize the growth in the line of puncture in gelatin and agar. Desiccated spores may survive for years. Anthrax spores are usually killed in four minutes by boiling temperature, but they vary in their resistance, and may withstand boiling temperature for twelve minutes (von Esmarch). Some anthrax spores are killed by 5 per cent. carbolic acid in two days; others survive for forty days. Various modifications of character of the anthrax bacillus can be produced by cultivation at high temperatures (42–43° C.) or by the addition of dilute antiseptics, the most important modifications being the production of an asporogenic variety of the bacillus and the loss of virulence. Any degree of attenuation of virulence can be produced down to complete loss. These attenuated cultures serve as vaccines to render animals insusceptible to anthrax. The anthrax bacillus is a facultative parasite. It is in the highest degree virulent for mice and

guinea-pigs, somewhat less so for rabbits. Sheep and cattle are the animals which suffer the most from the natural disease. Swine, dogs, and most birds are immune. Rats and pigeons are resistant, but not wholly insusceptible, to anthrax. Man does not rank among those highly susceptible to the disease. Infection may occur from the skin, intestine, or lungs. In small susceptible animals experimental anthrax is a septicæmia with abundant bacilli in the blood. In man anthrax usually occurs with localized inflammations at the seat of invasion (malignant pustule, intestinal anthrax, wool-sorter's disease). In some cases the disease remains localized; in others general infection and multiple localization occur.

Actinomyces, or Ray Fungus.—First recognized as a living organism by Bollinger in 1877 in actinomycosis or lump-jaw of cattle; observed in man in 1845 by B. von Langenbeck, whose discovery, however, was not published until 1878, when it was mentioned by J. Israel, to whom belongs the credit of first recognizing the ray fungus as a distinct microorganism pathogenic for man.

There are various species or varieties of the genus actinomyces, but we are able with our present methods to differentiate them from each other only imperfectly. Actinomyces hominis, which is probably identical with actinomyces bovis, is the only species which will be considered here. Authorities are not agreed as to the botanical position of this organism, but most writers now regard it as belonging to the group of the more highly-organized pleomorphic bacteria, and allied to cladothrix or streptothrix. Some, however, class actinomyces with the fungi.

Actinomyces is the cause of a chronic inflammatory affection, presenting sometimes the characters of an abscess, at other times more those of a tumor, with suppurating tracts and cavities. The presence of the parasite can usually be detected with the naked eye by finding in the pus small yellowish granules. These granules vary in size, shape, and color. They are usually described as about the size of a pin's head. They may be much smaller, even microscopic in size, and exceptionally they may be massed together in clumps the size of a pea. To the naked eye they generally appear round, but microscopically their contours are seen to be irregular. They may be grayish and translucent like sago particles, or opaque gray or white, or yellow, greenish-yellow, brownish, even black. Bostroem has demonstrated that these various tints depend partly upon the stage of development of the organism, the younger forms without club-like terminations being pale and transparent. The black granules have been observed only in intestinal actinomycosis. The consistence of the granules or colonies in their early stage of development is soft and gelatinous; later it becomes firm and compact, and it may become hard and gritty from deposit of lime salts in the old, degenerated colonies. The young, translucent bodies are most abundant in foci of rapid softening and liquefaction of the tissues. The number of the bodies present in the pus varies in different cases. They may be so few as to require long search to find them; usually they are numerous, and sometimes there are myriads of them.

These characteristic granules, visible to the naked eye, are colonies of the actinomyces or clumps of colonies. The youngest colonies are not visible to the naked eye. These consist of a central interlacing mass of

branching threads with radiating projections of threads. The most common and characteristic appearances are found in older colonies (called by the Germans "Drusen"). Here we find the centre of each colony composed of extremely fine interlacing threads and small round bodies resembling cocci, and the periphery made up of bulbous, club-like terminations of the threads. It is particularly this outer ring of radiating, club-shaped projections which gives to these bodies their most diagnostic feature. It requires careful study and differential staining to make out the real structure of the actinomyces bodies. Ordinarily, the central part of the colony appears simply as a confused granular and finely-filamentous mass. It has, however, been shown to consist of extremely delicate rods and threads, which branch dichotomously, and which, arranged somewhat loosely in the centre, become more densely interwoven and larger toward the periphery, and there pass in a radiating manner one into each of the swollen bulbs. This bulbous swelling appears to be due to an accumulation of a clear hyaline material in the sheaths of the fibres, and to represent only an involution or degenerative condition, not forming an essential part of the living structure of the parasite. The hyaline bulbs may present an appearance of concentric striation, and each one may break up into finger-like projections or have somewhat the appearance of a pine cone. They may become calcified. These are all degenerative changes. Both within and outside of the threads are seen round bodies like cocci, which are considered by Bostroem to be spores, but whose nature is undetermined. They may be very abundant, so that the central part of the colonies consists almost wholly of these round granules with very few threads. Cases of actinomycosis occur exceptionally in which there are no bulbous endings to the threads composing the colony. In addition to the colonies, numerous bacilli are often found scattered throughout the inflammatory nodules of actinomycosis. Pyogenic cocci are frequent secondary invaders in actinomycotic growths. Gram's and Weigert's fibrin stain and hæmatoxylin and eosin can be used to advantage in the microscopical study of actinomyces.

Many investigators claim to have cultivated the ray fungus. There is so much discrepancy in their descriptions of the characters and conditions of these cultures that we cannot recognize all of them as genuine cultures of actinomyces. Probably the most confidence is to be given to the cultures obtained by J. Israel and M. Wolff. They found that actinomyces grows best anaërobically and at the temperature of 35°–37° C. They used chiefly as their culture media nutrient agar and hen's and pigeon's eggs. The growth is slow and in the form of dry, small, projecting, irregular colonies, which are at first gray and translucent, and later opaque. On agar actinomyces grows chiefly in the form of rods—in eggs, in the form of interlacing, branching threads. Bulbous terminations of the threads are not observed in the cultures.

The majority of experimenters have obtained only negative results in attempting to produce actinomycosis experimentally in animals by inoculation of material containing the specific micro-organism. Bostroem in his elaborate article on actinomycosis considers all of the positive results reported up to the date of its publication (1890) as inconclusive. Since that date, however, several observers have reported more or less

success in producing the disease experimentally; and here, again, the results obtained by Israel and Wolff are the most noteworthy. They succeeded by introduction of their pure cultures of actinomyces into the peritoneal cavity of rabbits and guinea-pigs in producing small nodules in the peritoneum and spleen. These nodules contained typical actinomyces colonies with the bulbous rays. Further investigation is needed regarding the experimental inoculation of actinomyces.

Infection both of human beings and of cattle with actinomycosis has been often traced to the penetration of vegetable grains (wheat, barley, oats) or bits of vegetable fibre into the tissues. The portal of entry is frequently the mouth, particularly the neighborhood of the teeth, but it may be through a wound of the skin or through the mucous membranes of the throat, respiratory tract, œsophagus, intestine, or middle ear. It is not always possible to find the point of entrance, as this may heal completely.

Various clinical types of actinomycosis are recognized according to the seat of the affection, such as actinomycoses of the jaws and elsewhere about the head and neck, of the lungs, the pleura, the vertebræ, the intestine and other abdominal organs, the brain, the middle ear, the skin. There is usually a single localization, but there may be multiple foci, presenting sometimes anatomical and clinical characters of pyæmia.

The histological changes are characterized by necrosis and liquefaction of tissue with emigration of white blood-corpuscles as the immediate effect of the parasite, and a secondary reactive inflammation in the form of vascular granulation tissue. By some the changes are considered to be more closely allied to those of infectious granulomata than of ordinary inflammation. In some cases the process is rapid and destructive, with little new formation of tissue, and with the production of large abscesses; in others the affection may be very chronic, of limited extent, and encapsulated by new growth of tissue. When bone is involved there may be formed osteophytes and sclerosing ostitis, or there may be simply destruction without new formation of bone. Metastases do not appear to occur in the lymphatic glands communicating by the lymph-current with a primary focus of actinomycosis.

Madura disease, or mycetoma, both in the melanoid and the ochroid varieties, has been shown by Kanthack to be due to a parasite very closely allied to the ordinary actinomyces hominis. Kanthack considers that the parasite is simply a variety of the ordinary actinomyces.